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ONCOFETAL PROTEINS

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STRUCTURE/ IDENTIFICATION/ CHARACTERIZATION

1. MICROHETEROGENEITY OF ALPHA-FETOPROTEIN IN PATIENT SERUM AS DEMONSTRATED BY LECTIN AFFINO-ELECTROPHORESIS.

Breborowicz J, Mackiewicz A, Breborowitz D
Dept. Pathological Anatomy, Inst. Biostructure, 49, Przybyszewskiego St., 60355 Poznan, Poland
Scand J Immunol; 14(1):15-20 1981

Microheterogeneity of alpha-fetoprotein (AFP) present in the sera of 76 patients was studied by lectin affino-immunoelectrophoresis. Seventeen patients had benign liver disorders and the remaining 59 patients were treated for primary or secondary liver cancer or yolk sac tumor. By means of Con A, AFP was divided into two variants, while lentil lectin (LCA) made it possible to separate AFP in three variants. In some patients the relative concentrations of Con A and LCA AFP variants were similar; these patients were believed to produce AFP of the same 'profile'. Fourteen AFP profiles were observed by estimation of the area enclosed by precipitates corresponding to respective AFP variants. It was

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also possible to estimate the AFP profile on the basis of a simple visual analysis of the electrophoretic plates. The obtained results indicate that the AFP profiles of patients with cancer were variable. In spite of variations of the AFP profile in cancer patients, in most cases it was possible to differentiate primary liver cancer from yolk sac tumor and from liver metastases of cancer. In addition, in two-thirds of hepatoma patients the AFP profile was different from the profile observed in patients with benign liver disorders. (Author abstract) (17 Refs)

2. A NOVEL CELLULAR RETINOID-BINDING PROTEIN, F-TYPE, IN HEPATOCELLULAR CARCINOMA.

Muto Y, Omori M
First Dept. Internal Medicine, Gifu Univ. Sch. Medicine, Gifu City, Japan
Ann NY Acad Sci; 359:91-103 1981

The occurrence of the specific cellular retinol-binding protein previously identified in the fish-eye cytosol [CRBP(F)] was studied. [3H]-retinol binding assay showed the presence of CRBP(F) in 7/10 surgery specimens of hepatocellular carcinoma; CRBP(F) was detected in 4/5 patients with alpha-fetoprotein level of less than 200 nanog/ml. Vitamin A content in the tumor tissue was significantly lower than in the surrounding noncancerous tissue. The presence of CRBP(F) was also detected in the human fetal liver, in regenerating rat liver, and in hyperplastic liver nodules induced in rats by 2-acetylaminofluorene. CRBP(F) was found to be distinctly different from cellular retinoic acid-binding protein with respect to isoelectric point and relative electrophoretic mobility. These findings indicate that CRBP(F) can be considered as a novel onco-fetal protein, and that it is possible to prevent the experimental carcinogenesis by targeting retinoids to the hyperplastic nodules before hepatocellular carcinoma is established. (35 Refs)

3. ONCOFETAL ANTIGEN-I: DISTRIBUTION IN HUMAN TUMORS.

Rees WV, Irie RF, Morton DL
(c/o Irie) Div. Oncology, 54-140 CHS, Univ. California Los Angeles Sch. Medicine, Los Angeles, CA, 90024
JNCI; 67(3):557-562 1981

Oncofetal antigen-I (OFA-I) is a human tumor-associated fetal antigen that cross-reacts with fetal brain. The biological distribution of this antigen was studied in a variety of histologic types of human tumors and normal tissues. A total of 170 human tumors and 89 normal tissues obtained from biopsied and autopsied specimens were tested by immune adherence absorption assay. The antigen was most prevalent in malignant melanomas (82%); next in order of incidence were lung carcinomas (71%), sarcomas (61%), brain tumors (58%), and breast carcinomas (53%). However, OFA-I was found in only 15% of gastrointestinal tumors. The four hepatoma specimens tested were negative for OFA-I. OFA-I was also present in metastases and normal-appearing tissues of patients with OFA-I positive tumors but was not found in normal tissues from noncancer patients. These studies demonstrated that OFA-I is widely distributed among human tumors. It appears to be more prevalent in tumors of ectodermal and mesodermal origin. (Author abstract) (34 Refs)

4. PARTIAL CHARACTERISATION OF AN ONCOFETAL PANCREATIC ANTIGEN. ITS ROLE IN THE DIFFERENTIAL DIAGNOSIS AND THERAPY OF PATIENTS WITH PANCREATIC CANCER.

Knapp ML
Dept. Chemical Pathology, Westminster Medical Sch., London SW1P 2AR, England
Ann Clin Biochem; 18(3):131-142 1981

An assay for oncofetal pancreatic antigen (OPA) is described. Crossed-immunoelectrophoresis showed a single peak of alpha-2 mobility in the homogenates of fetal pancreas and in the serum and tumor homogenates of patients with pancreatic cancer. No reaction could be demonstrated in the tissue homogenates of fetal or adult liver, lung, stomach, colon, or esophagus. Immunoperoxidase technique showed the absence of staining in normal adult pancreas tissue. Staining was detected in the cytoplasm of pancreatic adenocarcinoma cells and in specimens of fetal pancreas. Rocket immunoassay showed the presence of OPA in the blood sera of the patients with pancreatic carcinoma; elevated OPA levels (greater than 6 units/ml) were recorded in 42/48 patients. OPA level in the blood sera of the patients with various other malignancies was significantly lower than that in the patients with pancreatic carcinoma. Sequential determinations in the patients with pancreatic carcinoma showed decrease of OPA level after curative resection, while the patients subjected to palliative treatment showed steady increase of OPA level with the advancement of the disease. (30 Refs)

ASSAY PROCEDURES/ SYNTHESIS

5. EVALUATION OF A RADIOIMMUNOASSAY MEASURING ACIDIC GLYCOPROTEIN LEVELS IN SERA OF BREAST CANCER PATIENTS (MEETING ABSTRACT).

Tokes ZA, Pullano TG, Lee YT, Shell WE
University of Southern California Comprehensive Cancer Center, Los Angeles, CA, 90033
4th Annual San Antonio Breast Cancer Symposium, Nov 6-7, 1981, San Antonio, Texas Cancer Therapy and Research Center of South Texas; 1981

A radioimmunoassay (RIA) was developed at Cedars-Sinai Medical Center using an acidic glycoprotein antigen isolated from neural tissue. The antigen has a subunit mol wt of 40,000+/-3,000. This assay was applied to a group of breast cancer patients (180) to evaluate its diagnostic potential. The normal values were 52.2+/-11.9 arbitrary units. Normal smokers exhibited av values which were 15% higher. Patients with primary infiltrating ductal carcinoma prior to treatment had a mean value of 59.7 with 6% positive. Patients with primary carcinoma and distant metastases prior to treatment had a mean value of 73.7 with 53% positive. Of the patients with distant metastases who have failed treatment, 41% were positive with a mean value of 77.7. The assay was positive for 11.9% of patients who were clinically identified with no evidence of disease. Patients with non-malignant conditions had a mean value in the normal value. Of the 45 patients who were carcinoembryonic antigen (CEA) positive, 11 (24.5%) were also positive in our RIA. Of the 23 patients who were CEA negative, 4 (17%) were positive in this assay. The potential usefulness of this RIA lies in monitoring the efficiency of various therapeutic modalities and in its inclusion in a panel of markers which would predict a gradual breakdown in three-dimensional tissue integrity. (no Refs)

EXPERIMENTS IN ANIMAL SYSTEMS

6. RAPID DEVELOPMENT OF LARGE NUMBERS OF ALPHA-FETOPROTEIN-CONTAINING 'OVAL' CELLS IN THE LIVER OF RATS FED N-2-FLUORENYLACETAMIDE IN A CHOLINE-DEVOID DIET.

Sell S, Leffert HL, Shinozuka H, Lombardi B, Gochman N
Dept. Pathology, Univ. California San Diego Medical Sch., La Jolla, CA, 92093
Gan; 72(4):479-487 1981

Fischer rats, fed 0.05% w/w N-2-fluorenylacetamide in a choline-devoid diet for 2 wk, developed a massive infiltration of the liver by small 'oval' cells. This occured rapidly 1 wk after feeding the diet for 2 wk. All of the rats fed the choline-devoid diet died within 5 wk, with massive oval cell infiltration of the liver. Although similar changes occurred in rats fed N-2-fluorenylacetamide in a choline-supplemented diet, the degree was much less. In rats fed a choline-devoid diet without N-2-fluorenylacetamide, proliferation of hepatocytes, but not of oval cells, was observed. Because the carcinogen-enhancing effects of choline-devoid diets seem to exceed those of partial hepatectomy, such diets may work by causing changes distinct from those induced by partial hepatectomy. Many oval cells contain alpha-fetoprotein, and the rapid oval cell increase is associated with an exponential increase in serum alpha-fetoprotein concentration. These observations suggest that a cellular change, not an alteration of gene expression in parenchymal cells, is the primary cause of hyper-alphafetoproteinemia during the course of chemical carcinogenesis in rats. (Author abstract) (40 Refs)

7. RELATIONSHIP OF ALPHA FETOPROTEIN AND ALPHA MACROFETOPROTEIN SYNTHESIS TO NORMAL AND MALIGNANT HEPATOCELLULAR PROLIFERATION.

Smalley JR
State University of New York, Buffalo, NY
Diss Abstr Int (B); 42(1):90-B 1981

Intracellular alpha fetoprotein and alpha macrofetoprotein synthesis was demonstrated in both Zajdela rat ascites hepatoma cells, and hepatocytes from regenerating rat liver. Previously, both these proliferating liver cell types had been considered nonproducers of alpha fetoprotein and alpha macrofetoprotein. The synthesis of alpha fetoprotein by these replicating liver cells did not result in its secretion into either the culture fluid in vitro, or the serum in vivo. However, alpha fetoprotein was demonstrated to localize at the cell surface of the ascites hepatoma cells. Failure of these replicating hep atocytes to secrete rather than to produce alpha fetoprotein satisfactorily explains the previous failure to detect elevated alpha fetoprotein levels in either of these systems. Synthesis studies using either pharmocologically synchronized Zajdela ascites hepatoma cells or regenerating rat hepatocytes revealed that both alpha fetoprotein and alpha macrofetoprotein are synthesized prior to deoxyribonucleic acid. The results of these investigations indicate that a temporal relationship exists between alpha fetoprotein and deoxyribonucleic acid synthesis during hepatocyte regeneration, and hepatoma growth. This temporal relationship is consistent with the conclusion that a causal relationship exists between intracellular onset of alpha fetoprotein synthesis and hepatocellular proliferation. No such relationship apparently exists for synthesis of alpha macrofetoprotein. (no Refs)

8. IMMUNOHISTOCHEMICAL STUDIES OF ALPHA-FETOPROTEIN- AND ALBUMIN-CONTAINING CELLS IN THE LIVER DURING ONTOGENESIS AND THE EARLY STAGE OF 3'-METHYL-4-DIMETHYLAMINOAZOBENZENE (3'ME-DAB) HEPATOCARCINOGENESIS.

Sasaki M, Dempo K, Kaku T, Satoh M, Mori M
Second Dept. Pathology, Sapporo Medical Coll., Sapporo-shi, Hokkaido 060, Japan
Kanzo; 22(2):254-265 1981

Single and simultaneous occurrence of alpha-fetoprotein (AFP) and albumin (ALB) in the liver of rat fetuses, neonatal rats and rats fed a 3'methyl-4-dimethylaminoazobenzene (3'Me-DAB) diet was studied by the peroxidase-labeled antibody method. In the very early stage of hepatocarcinogenesis, when maturation from oval cells to transitional cells began to occur, only AFP was found in the scant cytoplasm of transitional cells. In a more advanced stage, when maturation from oval cells to transitional cells and small hepatocytes occurred frequently, simultaneous presence of AFP and ALB was observed in those cells. When small hepatocytes assumed the appearances of hepatocytes, only ALB was found in them. By day 12 of gestation, AFP and ALB were already present in all hepatocytes. This tendency continued during the entire fetal life. After birth, AFP-containing cells gradually disappeared from the periphery of the hepatic lobe toward the central area. Finally, all hepatocytes contained only ALB. The fluctuation of AFP and/or ALB-containing cells in the early stage of 3'Me-DAB hepatocarcinogenesis was very similar to that of ontogenesis of rat liver. That is, the former retraced the process of ontogenic differentiation of the liver. (46 Refs) (In JPN)

9. ENHANCEMENT OF PLASMA ALPHA-FETOPROTEIN, AS MEASURED BY SANDWICH-TYPE RADIOIMMUNOASSAY, AND INDUCTION OF GAMMA-GLUTAMYL TRANSPEPTIDASE-POSITIVE HEPATIC CELL FOCI IN RATS FED BENZO(A)PYRENE.

Boyd JN, Stoewsand GS, Misslbeck N, Campbell TC, Mason R, Lepp CA, Odstrchel G
(c/o Stoewsand) Dept. Food Science and Technology, New York State Agricultural Experiment Station, Geneva, NY 14456
J Toxicol Environ Health; 7(6):1025-1035 1981

The ability of dietary benzo(a)pyrene (BaP), a known carcinogen not strongly associated with hepatocarcinogenesis, to cause early alpha-fetoprotein (AFP) elevation and/or induction of gamma-glutamyl transpeptidase (GGT)-positive liver cell foci was studied. The radioimmunoassay technic for AFP is described. Sixty weanling male Fischer rats were divided into four equal groups and were fed diets containing 0, 1, 100, or 1,000 ppm BaP. Radioimmunoassay validation is described. The group of rats consuming 1,000 ppm BaP had lower body weights by wk 1. The 0, 1, and 100 ppm groups showed no differences until wk 13 when the 100 ppm groups exhibited a slight depression in body wt. AFP concentrations declined with increasing age through wk 13. There were no differences among treatment groups during the first 4 wk, but during wk 5 and 6, AFP concentrations were significantly higher in the 1,000 ppm group. No differences were observed in the groups receiving 0, 1, or 100 ppm BaP during wk 7-13. Four animals fed 1,000 ppm BaP for 5 wk showed dense staining of GGT activity in the bile duct and discrete foci, 10-20 cells in diameter, primarily near the major artery within the central part of the lobe. Bile duct proliferation was also apparent. Sections from control animals showed dense staining in the bile ducts with no proliferation. Animals fed 0, 1, or 100 ppm BaP showed essentially no difference in staining for GGT activity. No foci were apparent. Bile ducts showed greater than normal activity, with some possible proliferation in all animals. All BaP-treated rats showed centrilobular fat accumulation. (31 Refs)

10. SERIALLY TRANSPLANTED HUMAN STOMACH CANCER PRODUCING ALPHA-FETOPROTEIN (AFP) IN NUDE MICE.

Nakatani K, Ezaki T, Miyagi N, Shiratori T, Konishi Y, Kozima K
First Dept. Surgery, Nara Medical Univ., Kashihara-shi, Nara Pref. 634, Japan
Igaku Ayumi; 116(2):87-89 1981

The primary lesion (Borrman's type II, poorly differentiated adenocarcinoma, macroscopical findings of no dissemination peritoneal metastasis, no liver metastasis, lymph node metastasis to lymph node group 1, and definite invasion to the serosa; Stage III) of a patient whose preoperative serum AFP concentration was not determined, but who had a serum AFP concentration of 93 ng/ml 7 mo after radical surgery when a local relapse was seen, and of 136 ng/ml 1 mo later, was removed from the gastric serosa by wedge-shaped resection. The tumor was minced and two or three pieces were transplanted into the backs of 6-to 8-wk-old male nu/nu/ mice. Serial transplantation was performed in the same way. Blood was obtained and the mice were killed after the tumors were at least 100 mm2, in the 7th-12th generation. The AFP in the tissue of a serially transplanted tumor of about 1 g at the time of killing in the 11th and 12th generation was measured by radioimmunoassay. The growth rate of the transplanted tumor increased with advance of the serial generation, and the tumor size became uniform. The serum AFP values for the 7th, 8th, 9th, 10th, 11th, and 12th generations were 155 ng/ml, 35 and 419 ng/ml, 160 ng/ml, 205 ng/ml, 216 ng/ml, and 552 and 696 ng/ml, respectively. The AFP concentration increased with enlargement of the tumor in all generations. The AFP concentration in the tissue was 5.36 ug/g and 9.72 ug/g for the 11th and 12th generations, respectively, while that in the controls was 0.4 ug/g and 0.27 ug/g, respectively. (7 Refs) (In JPN)

11. DIFFERENTIAL LOCALIZATION OF HUMAN PANCREAS CANCER-ASSOCIATED ANTIGEN AND CARCINOEMBRYONIC ANTIGEN IN HOMOLOGOUS PANCREATIC TUMORAL XENOGRAFT.

Tan MH, Shimano T, Chu TM
(c/o Chu) Dept. Diagnostic Immunology Res. and Biochemistry, Roswell Park Memorial Inst., 666 Elm St., Buffalo, NY, 14263
JNCI; 67(3):563-569 1981

Tissue localization of a human pancreas cancer-associated antigen (PCAA) and carcinoembryonic antigen (CEA) was studied in a homologous pancreatic tumoral xenograft, a human pancreatic cancer line established from ascites (AsPC-1), with the use of the indirect immunofluorescence technique with specific anti-PCAA and anti-CEA antisera. Histologically, AsPC-1 xenograft was composed of mucinous adenocarcinoma of variable size and degree of glandular differentiation. PCAA was selectively associated with the columnar cytoplasm, was involved primarily in the epithelial proliferation, and originated at the basal aspect of the glands. In contrast, CEA appeared diffuse and was found predominantly in the cuboidal cells, with higher intensity at the luminal border and in mucin. Furthermore, growth comparison of the AsPC-1 adenocarcinoma revealed that, except in the juvenile gland that was morphologically consistent with Grade 1 (G1) carcinoma in situ, the number of PCAA-positively stained cells decreased from G1 to Grade 4 epithelial differentiation. In well-differentiated adenocarcinoma and degenerating adenocarcinoma, cells positive for PCAA were released into the lumen of the glands, whereas in poorly differentiated adenocarcinoma these cells were often scattered singly and/or in focal clusters and disappeared in very poorly differentiated adenocarcinoma. This study showed that the pCAA was different from CEA in its immunologic reactivity and distribution in its homologous tumoral tissues, in which PCAA was predominantly associated with the proliferative phase of the malignant epithelium. These results also indicated the potential applicability of this antigenic expression in the etiology, disease grading, and staging of human pancreatic cancer. (Author abstract) (16 Refs)

CLINICAL/ DIAGNOSIS/ IMMUNOTHERAPY

12. TUMOUR MARKERS: THEIR ROLE IN CLINICAL MEDICINE.

Dearnaley DP, Coombes RC

Clinical Oncology Unit, Ledwig Inst. Cancer Res. (London Branch), Royal Marsden Hosp., Sutton, Surrey, England

Practitioner; 225(1356):839-841,843-844,846-849 1981

Biochemical tumor markers currently used in diagnosis and monitoring responses to treatment are human chorionic gonadotropin (HCG) in trophoblastic tumors; beta subunit HCG and alpha-fetoprotein (AFP) in testicular tumors; AFP (if the initial titer is very high) in hepatomas; acid phosphatase in prostatic cancer; catecholamines in neuroectodermal tumors; and calcitonin in medullary carcinoma of the thyroid. Carcinoembryonic antigen (CEA) assays are useful for monitoring responses to treatment in patients with colorectal cancer, but cannot be used in diagnosis. Certain lung tumors (especially oat cell carcinomas) secrete ectopic ACTH, antidiuretic hormone, and/or calcitonin. These ectopic hormones may also be present in patients with chronic obstructive pulmonary disease, but the ectopic hormones associated with lung cancer are often of abnormally high mol wt. Assays for these high-mol wt hormones may be useful for monitoring responses to therapy. Adenocarcinomas and squamous cell carcinomas of the lung may produce CEA, alkaline phosphatase, and gamma-glutamyl transpeptidase. However, elevated CEA levels are present in smokers and patients with many non-neoplastic and inflammatory diseases, and the enzymes are not tumor-specific. At present, the role of biochemical markers in the management of the common solid tumors is rather limited. The use of tumor markers in breast and lung cancer must await further research. Monoclonal antibody technology should soon provide satisfactory antibodies for immunolocalization and immunocytochemistry studies in breast cancer patients. (12 Refs)

13. CARCINOEMBRYONIC ANTIGEN LEVELS AS AN INDICATOR OF THE PRIMARY SITE IN METASTATIC DISEASE OF UNKNOWN ORIGIN.

Koch M, McPherson TA
Dept. Medicine, Cross Cancer Inst., 11560 University Ave., Edmonfon, Alberta, T6G 1Z2, Canada
Cancer; 48(5):1242-1244 1981

In 542 patients with metastatic disease arising from a known primary site, elevated CEA levels (greater than 10 ng/ml) were most often associated with metastatic disease originating from entodermally derived organs, breast, and mucinous ovarian primaries. This observation held true, in general, in a small series of 32 patients with metastatic disease arising from a primary site that had been unknown, but that was eventually identified. Thus, although a CEA level below 10 ng/ml is of no use in pointing to a particular primary site, a value above 10 ng/ml suggests the site is more likely to be in an entodermally derived organ, breast or ovary containing a mucinous carcinoma. If liver metastases are present, there is an increased probability that the primary site will be found in the large bowel or pancreas. (Author abstract) (9 Refs)

14. CARCINOEMBRYONIC ANTIGEN IN THE MANAGEMENT OF GASTRIC CANCER PATIENTS.

Tomoda H, Furusawa M, Ohmachi S, Seo Y, Matsukuchi T, Miyazaki M, Kanashima R
Dept. Surgery, Natl. Kyushu Cancer Center, 595, Notame, Minami-ku, Fukuoka 815, Japan
Jpn J Clin Oncol; 11(1):69-74 1981

The results of investigations on carcinoembryonic antigen (CEA) levels in 226 patients with gastric cancer (73 Stage I, 12 Stage II, 71 Stage III, and 70 Stage IV) and the usefulness and limitations of their determination are described. The primary lesion was resectable in 203 cases (148 curative and 55 noncurative resections) and unresectable in 23 cases. Preoperatively, elevated CEA levels (5 ng/ml or higher) were found in 23.9% of the patients. The levels were high in 56.5% of the patients with unresectable tumors and in 20.2% of those with resectable tumors. Elevated levels were found in 34.5% of the patients receiving noncurative surgery and in 14.9% of those who had curative surgery. Elevated CEA levels were found in 8.2% of the patients in Stage I, 25% in Stage II, 23.8% in Stage III, and 40% in Stage IV. The differences between Stages I and III and I and IV were significant. Elevated CEA levels were found in 68.6% of the 16 patients with liver metastasis, and in 20.5% of the 210 patients without liver metastasis. In 24 patients who had high CEA levels before gastrectomy (12 curative and 12 noncurative), the CEA levels 1 mo after surgery were normal in 10 of the patients receiving curative surgery and in 1 of the patients receiving noncurative surgery. (28 Refs)

15. GASTRIC ULCER, GASTRITIS AND GASTRIC CARCINOMA.

Maaroos HI, Salupere V, Uibo R
Tartu State Univ., Tartu, Esthonian SSR, USSR
Ann Clin Res; 13(3):151-153 1981

The gastritis-gastric ulcer relationship and the incidence of gastric carcinoma and the level of serum carcinoembryonic antigen (CEA) in benign gastric ulcer were investigated. A series of 112 patients were subjected to endoscopic examination 1-4 yr after diagnosis of gastric ulcer. There were 72 men and 40 women; mean age 50.6, range, 25-75 yr. Examination revealed chronic gastritis in 102/112 (91%) and isolated antral gastritis in 48% (superficial in 12%, atrophic in 36%). Pangastritis was found in 42% of the cases but isolated fundal gastritis was found in only one case. In 10 cases both the fundal and antral mucosa were normal and in one case the antral mucosa only was normal. During the 2-4 yr observation period, gastritis developed or progressed in 20 (31%) and improved in 11 (17%) of the 64 reexamined cases. Eight of the 11 normal antral mucosa cases remained normal. During the observation period, five patients died and 11 were operated on. Gastric carcinoma was diagnosed during the observation period in four cases, 1-27 mo after the first examination. The blood level of CEA was greater than 10 nanog/ml in 17/56 gastric ulcer cases and in 13/91 controls. CEA activity remained elevated in 11/12 of these gastric ulcer cases when the level was determined about 3 yr later. (16 Refs)

16. LOCALIZATION AND CONCENTRATION OF CARCINOEMBRYONIC ANTIGEN (CEA) IN GASTROINTESTINAL TUMORS: CORRELATION WITH CEA LEVELS IN PLASMA.

Wagener C, Muller-Wallraf R, Nisson S, Groner J, Breuer H
(c/o Breuer) Institut fur Klinische Biochemie, Sigmund-Freud Strasse 25, 5300 Bonn 1, W. Germany
JNCI; 67(3):539-547 1981

In 50 patients with gastrointestinal carcinomas, the following tumor parameters were studied: the concentration and localization of carcinoembryonic antigen (CEA) in tissue, extension, invasion, infiltration, differentiation, and necrosis. CEA concentrations were measured in plasma samples of all patients. In seven patients with gastric carcinomas, CEA concentrations in tissue were low. Generally, only single cells or cell groups were CEA-positive. Elevated CEA levels in plasma resulted mainly from distant metastases and not from the primary tumor. In 43 colorectal carcinomas, CEA concentrations in tissue varied between 1.5 and 472 ug/g tissue. They were closely related to the degree of accumulation of CEA-positive necrotic material in the neoplastic glands. In 35 patients with colorectal carcinomas without CEA producing distant metastases, preoperative CEA levels in plasma were normal when tumor necrosis and perineural invasion were absent and CEA concentrations in tissue were low. CEA levels in plasma were regularly elevated when the tumor showed considerable necrosis in the presence of high CEA concentrations in tissue. (Author abstract) (22 Refs)

17. FURTHER INVESTIGATIONS OF IMMUNOREACTIVE CARCINOEMBRYONIC ANTIGEN (CEA) IN COLORECTAL CANCER PATIENTS - WITH PARTICULAR EMPHASIS ON THE CORRELATION BETWEEN IMMUNOREACTIVE CEA LEVELS IN TISSUE, FECES AND BLOOD.

Fujimoto S, Kitsukawa Y
First Dept. Surgery, Sch. Medicine, Chiba Univ., Chiba, Japan
Jpn J Surg; 11(1):27-32 1981

The relationship between the level of immunoreactive carcinoembryonic antigen (IR-CEA) in the tissues, feces and blood was studied in 14 patients (aged 46 to 71 yr) with colorectal cancer. The level of IR-CEA in the tumor tissue was almost 30x greater than that in the normal colonic mucosa. IR-CEA content in well differentiated adenocarcinoma was greater than that in moderately differentiated adenocarcinoma. Total tumor IR-CEA level calculated as the product of the estimated tumor wt by tumor IR-CEA level was found to show a definite correlation with the serum and fecal IR-CEA levels. (21 Refs)

18. VALUE OF CARCINOEMBRYONIC ANTIGEN (CEA) IN THE DIAGNOSIS AND POSTOPERATIVE MONITORING OF PATIENTS WITH COLORECTAL CANCER.

Catania G, Basile F, Cardi F, Azzarello G, Mazzarino C, Campo M, Giovinetto A
I Clinica Chirurgica, Universita di Catania, Catania, Italy
Minerva Chir; 36(9):569-580 1981

Ther serum CEA levels were monitored in 88 patients with colorectal carcinoma, who were submitted to radical surgery. Before surgery, the CEA levels were elevated (exceeding 20 nanog/ml) in Stage B, in 87.5% in Stage C, and in 60% in Stage D. Preoperatively normal or nearly normal CEA levels showed no significant changes after surgery. The incidence of metastases and local recurrences was higher among the patients with preoperatively high CEA levels. After surgery, the CEA levels were elevated in 60% of the patients who developed local recurrences and in all patients who developed metastases. The postoperative increase in the CEA level was considerable and rapid in the patients developing metastases, especially hepatic metastases, preceding the clinical manifestation of the metastases by up to several mo. The rise preceding the development of local recurrence was slower. (53 Refs) (In ITA)

19. THE USEFULNESS AND LIMITATIONS OF CEA ASSAY IN THE MANAGEMENT OF COLORECTAL CANCER.

Tomoda H, Furusawa M
Dept. Surgery, Natl. Kyushu Cancer Center, Fukuoka 815, Japan
Jpn J Surg; 11(1):33-38 1981

The prognostic value of carcinoembryonic antigen (CEA) assay was studied in 171 patients with colorectal cancer. Pre- and postoperative CEA levels were determined in 90/171 patients. Preoperative plasma CEA level of greater than 5.0 nanog/ml was recorded in 51.1% of the patients (37.7% of the patients subjected to radical resection, 67.7% of the patients subjected to palliative resection, and 75.0% of unresectable patients). Postoperatively, CEA levels returned to normal values in 94.7% of the patients subjected to radical resection, compared with 57.1% after palliative resection and 33.3% after exploratory surgery. Of 28 patients with recurrences, 24 had CEA levels of greater than 5 nanog/ml. The patients with liver metastases had CEA levels of greater than 10 nanog/ml. (18 Refs)

20. CORRELATION OF PLASMA CEA AND CEA TISSUE STAINING IN POORLY DIFFERENTIATED COLORECTAL CANCER.

Goslin R, O'Brien MJ, Steele G, Mayer R, Wilson R, Corson JM, Zamcheck N
(c/o Zamcheck) Mallory Gastrointestinal Res. Lab., Boston City Hosp., Boston, MA, 02118
Am J Med; 71(2):246-253 1981

A review of patients operated on for colorectal cancer disclosed poorly differentiated histologies in those whose preoperative and postoperative carcinoembryonic antigen (CEA) levels were not elevated, even in the presence of metastatic disease. CEA was, therefore, of little prognostic value or predictive of disease recurrence in these patients. The amount of CEA in tumor tissue of 17 patients with poorly differentiated colorectal cancer was estimated with the immunoperoxidase staining technique and was correlated with histology and plasma CEA levels obtained during various stages of disease. Five tumors did not stain negatively for CEA and all had predominantly poorly differentiated histologies. In all of these patients metastatic disease developed but not elevated plasma CEA levels. In contrast 12 tumors stained positively for CEA and were found to contain either differentiated areas or signet ring cells. Serial plasma CEA levels correctly monitored the postoperative courses of all 12 patients. Six of these had a relapse and all were detected by serial increases in plasma CEA. The remaining six were disease free greater than 48 mo after resection and had normal plasma CEA levels. Among poorly differentiated tumors, those that contain gland-forming areas of signet ring cells can be assumed to produce CEA, and plasma CEA levels can be used effectively for monitoring. On the other hand, undifferentiated tumors which do not stain for CEA identify those patients whose plasma CEA levels do not provide a useful monitor. (Author abstract) (25 Refs)

21. CORRELATIONS BETWEEN SERIAL CEA LEVELS AND SURGERY IN PATIENTS WITH COLORECTAL CARCINOMA.

Midiri G, Amanti C, Benedetti M, Caliento D, Consorti F, Del Buono S, Di Paola M
(c/o Amanti), Clinica Chirurgica IV, Policlinico Umberto I, 00185 Roma, Italy
J Surg Oncol; 17(4):341-344 1981

Nowadays the evaluation of serial carcinoembryonic antigen (CEA) levels represents an important parameter for the prognosis of patients with carcinoma of the large bowel. Changes in CEA values allow the drawing of conclusions regarding the effectiveness of therapy. We have studied 63 patients with colorectal carcinoma that underwent surgical treatment. Serial CEA levels were tested in each patient before surgery and 15 days after. The 53 patients were considered surgically cured; and among these 7 did not have a significant decrease of CEA values after surgery. The percentage of recurrences among these patients has been 71.4%; meanwhile patients who showed a decrease of CEA values below cutoff values had recurrences only in 17.3% of cases. For this reason it is our opinion that patients considered surgically cured who have postoperative high CEA levels cannot be considered really cured from a biological point of view. (Author abstract) (19 Refs)

22. PLASMA CARCINOEMBRYONIC ANTIGEN IN THE DIAGNOSIS AND MANAGEMENT OF PATIENTS WITH HEPATOCELLULAR CARCINOMA.

Melia WM, Johnson PJ, Carter S, Munro-Neville A, Williams R
Liver Unit, King's Coll. Hosp. and Medical Sch., Denmark Hill, London SE5 8RX, England
Cancer; 48(4):1004-1008 1981

The value of serial carcinoembryonic antigen (CEA) measurements as a marker of disease progression or in monitoring treatment was investigated in patients with hepatocellular carcinoma. Of 40 patients, including 16 with normal serum alphafetoprotein (AFP) concentrations, 29 (72.5%) had abnormal plasma CEA at presentation. Although this was more common in patients with pre-existing cirrhosis, the mean and range of plasma CEA were similar in patients with and without pre-existing hepatic disease. There was no correlation between plasma CEA and any biochemical parameter of hepatic function, although plasma CEA concentrations were significantly lower in patients with well-differentiated tumors. CEA concentrations increased in 71% of patients who had no response to cytotoxic drugs, but CEA also increased in 62.5% of those patients who did respond. Plasma CEA concentrations were elevated in 62.5% of patients with normal and 79% of patients with raised serum AFP on admission to the hospital. There was no correlation between individual AFP and CEA concentrations. Although elevated plasma CEA levels may be of diagnostic value in patients with hepatocellular carcinoma in the absence of pre-existing hepatic disease, and in those with normal serum AFP, our findings indicate that it does not behave as a true tumor marker. (Author abstract) (11 Refs)

23. SIGNIFICANCE OF CARCINOEMBRYONIC ANTIGEN IN THE DIAGNOSIS OF LIVER DISEASES.

Fiaccadori F, De Simoni M, Ghinelli F, Magnani G, Pelsoi G, Salvadoin C
Cattedra di Malattie Infettive, Univ. Parma, Parma, Italy
Minerva Med; 72(28):1847-1854 1981

Carcinoembryonic antigen (CEA) measurements performed on 419 patients with acute and chronic diseases of varying etiology and severity, and benign or malignant obstructive icterus, are presented. CEA data of liver diseases with major functional damage, do not differentiate cirrhosis and Ca-cirrhosis, or between benign and malignant icterus. (34 Refs) (In ITA)

24. CLINICAL EVALUATION OF CARCINOEMBRYONIC ANTIGEN (CEA) LEVELS IN SERUM AND TUMOR TISSUE OF BREAST CANCER PATIENTS.

Kitamura M, Tominaga T, Kaneko H, Hayashi K, Takahashi I, Saito T, Ito I
Dept. Surgery, Tokyo Metropolitan Komagome Hosp., Tokyo, Japan
Nippon Gan Chiryo Gakkai Shi; 16(1):35-43 1981

CEA was studied in 236 patients with primary breast carcinoma, 51 with recurrent breast carcinoma, and in 14 with benign breast disease. Levels of serum CEA greater than 2.5 nanog/ml were observed preoperatively in 23/216 patients with Stage I, II, or III primary breast cancer, and postoperative increases in the levels of CEA were thought to indicate the possibility of distant metastasis. Levels of CEA greater than 2.5 nanog/ml were also observed in 11/20 patients with Stage IV primary breast cancer patients and 22/51 patients with recurrent breast cancer. Some associations were observed between the therapeutic results of particular therapies and levels of serum CEA in 25 patients with advanced breast cancer who se levels of serum CEA were determined serially before and after treatment. Serum CEA levels were highest in patients with liver metastasis as the primary site of recurrence. Levels of CEA in tumor tissues were not related to the clinical stage of the cancers, the degree of axillary lymph nodal metastasis, histological type of the tumors, pre- or postmenopausal status of the patients, or number of estrogen receptors in the tumor tissue. All of the patients who were observed to have high levels of serum CEA also had high levels of CEA in tumor tissue, and patients with high levels of CEA in tumor tissues were thought likely to have elevated CEA levels during periods of postoperative recurrence. (16 Refs) (In JPN)

25. PROGNOSTIC SIGNIFICANCE OF ELEVATED PREOPERATIVE CEA LEVELS IN PRIMARY BREAST CANCER PATIENTS (MEETING ABSTRACT).

Hager JC, Furmanski P, Ownby H, Roi L, Brennan MJ, Rich MA
AMC Cancer Research Center and Hospital, Lakewood, CO, 80214
4th Annual San Antonio Breast Cancer Symposium, Nov 6-7, 1981, San Antonio, Texas Cancer Therapy and Research Center of South Texas; 1981

The prognostic significance of serum carcinoembryonic antigen (CEA) levels has been assessed retrospectively in 233 Stage I and II primary breast cancer patients. Study patients had negative bone scans and a mean number of 14 lymph nodes excised and examined at mastectomy, and were asymptomatic at 3 mo post-surgical follow-up intervals. CEA levels were determined by the Abbott Laboratories solid phase enzyme immunoassay in which CEA levels greater than 4 ng/ml are considered abnormal. Prognostic significance was determined by the correlation between assay value and the recurrence rate at 24 mo after mastectomy using life table analysis. Of the 233 women studied, 198 were disease-free with a mean follow-up period of 27 mo, and 35 experienced recurrence of disease with a mean time to recurrence of 16.5 mo. Two hundred study patients had normal preoperative CEA values, and 33 had elevated ones. There was a significant difference in the recurrence rate for patients with normal CEA values compared with those with elevated CEA values. Further analysis stratified patients by estrogen receptor values and by lymph nodes status. Elevated CEA levels could be correlated with earlier recurrence in estrogen receptor positive and negative patients as well as in patients with positive and negative lymph node status. Thus, it would appear that elevated CEA values determined at the time of primary treatment are predictive of early recurrence. (no Refs)

26. THE CEA TEST IN BREAST CANCER.

Breslin BK, Healy JB
Saint Luke's Hosp., Dublin 6, Ireland
Ir Med J; 74(7):203-204 1981

Carcinoembryonic antigen (CEA) was measured in 111 patients with breast cancer. Operable cancers had all been treated by mastectomy before CEA measurements. Serial estimations of CEA titers were performed at approx 3 monthly intervals and all patients were followed for at least 2 yr. Forty patients had initial CEA titers of greater than 10 nanog/ml: 22 had either grossly residual or recurrent carcinoma, or had demonstrable metastases; 18 had no detectable cancer. Fourteen of these latter patients developed metastases from 3-31 mo after the finding of the elevated CEA titer. Seventy-one patients initially had a CEA titer less than 10 nanog/ml: 17 had either residual carcinoma or demonstrable metastases; while 48 continued to be well and six developed metastatic disease from 3-11 mo after a rise in CEA titer was found. A low CEA titer does not exclude neoplasm, but taken in conjunction with other clinical signs of early disease it improves the prognosis and may spare the patient a long course of chemotherapy. (7 Refs)

27. CEA IN CARCINOMA OF THE BREAST (MEETING ABSTRACT).

Biscottini B, Buzzi F, Di Costanzo FF, Grignani F
Servizio Oncologico della Clinica Medica, Ospedale Civile S Maria, Terni, Italy
Tumori; 67(2,SupplA):217 1981

In the Oncologic Service of the Medical Clinic of Terni Hospital, 576 carcinoembryonic antigen (CEA) determinations (Sorin radioimmunoassy [RIA] method) were made in 129 patients (pat) with breast cancer. CEA levels were reduced in 27/31 pat following mastectomy, however the difference is not statistically significant; stage II N-: CEA reduced in 13/14 (2 +/-1.42 ng/ml vs 1.59 +/-1.52), stage II N+: reduced in 11/14 (4.51 +/-2.92 ng/ml vs 4.4 +/-4.14), stage III N+: reduced in 3/3 (4.86 +/-1.61 vs 2.2 +/-1.44). Av values (AV) were elevated in direct proportion to the stage of the disease: in 30 pat in stage II (N-) the AV is 1.87 +/-1.48; in 50 pat in stage II (N+) the AV is 2.43 +/-1.31; in 8 pat in stage III the AV is 3.34 +/-1.66; in 41 pat in stage IV the AV is 16.53;

however 17 of these pat had levels below 6 ng/ml. 8 out of 80 with low AV (stage II AV 1.85 +/-0.58) developed metastases at the same time their antigen levels increased (AV 4.23 +/-1.65 with (p greater than 0.5). 9 pat in adjuvant therapy showed a drop in AV from 4.28 +/-2.98 to 0.98 +/-0.68. No spontaneous reductions were recorded in any untreated patients. The AV of CEA turned out proportional to the stage of the disease even though 41 per cent of pat in stage IV had values within normal limits; pat who developed metastases had a simultaneous rise in CEA; patients in adjuvant therapy showed a decrease in CEA no changes were observed in them in clinical follow-up. Our conclusions which have been deduced from a limited number of patients require further confirmation. (no Refs) (In ITA)

28. CLINICO-PROGNOSTIC CORRELATIONS BETWEEN CIRCULATING IMMUNE COMPLEXES AND CARCINOEMBRYONIC ANTIGEN IN CARCINOMA OF THE BREAST (MEETING ABSTRACT).

Marini G, Bonfanti V, Rossi G, Verzura P, Balestrieri G, Tinacani A, Robustelli Della Cuna G
III Div. Medicina Generale, Spedali Civili, Brescia, Italy
Tumori; 67(2,SupplA):199 1981

In inoperable breast cancer, as in other neoplasms, the presence of circulating immune complexes (IC) seems to be an unfavorable prognostic factor. We present the results of IC evaluation in 86 breast cancer patients of whom 34 are apparently disease-free following mastectomy and 52 have advanced disease. The IC were investigated by 2 complementary methods, the C1q-BA and the KgB-SP. The patients with no signs of disease had a higher percentage positive for IC, although not significantly, than the group with advanced disease (41.2 per cent vs 28.8 per cent). The presence of IC was not related to any prognostic factor (age, menopausal status, clinical stage, type of metastases) nor to the presence of carcinoembryonic antigen (CEA) tested for in the serum (radioimmunoassay [RIA]-Sorin) of 58 patients and found to be significantly elevated (P less than 0.01) in patients with advanced disease (58.8 per cent) compared to the group with no signs of disease evident (16.6 per cent) . It was impossible to establish a relation between the presence of IC and serum CEA values, a fact which seems to shed doubt on CEA involvement as an antigenic component of IC. (2 Refs) (In ITA)

29. SIGNIFICANCE OF SIALIC ACID AND CARCINOEMBRYONIC ANTIGEN AS MONITORS OF TUMOR BURDEN AMONG PATIENTS WITH CARCINOMA OF THE OVARY.

Silver HK, Karim KA, Salinas FA, Swenerton KD
Advanced Therapeutics Dept., Cancer Control Agency British Columbia, Vancouver, British Columbia, Canada
Surg Gynecol Obstet; 153(2):209-213 1981

Serum sialic acid may serve as a valuable tumor marker for a variety of malignant neoplasms. To evaluate the clinical significance in carcinoma of the ovary, both sialic acid and carcinoembryonic antigen were measured in 69 patients with carcinoma of the ovary. Eligible patients all had assessable tumor burden: in group I, 11 patients had no evidence of disease 4 to 8 wk after surgical assessment; in group II, 21 patients had no tumor more than 2 cm in diameter; and in group III, 37 patients had advanced disease. While intergroup comparisons for carcinoembryonic antigen showed no differences between tumor burden groups, sialic acid was significantly related to tumor burden by the same pairwise statistical analysis. Of the 58 patients with demonstrable tumor burden, 36 demonstrated sialic acid elevations as compared with 13 elevations for carcinoembryonic antigen. During serial follow-up study, there were 41 episodes of objective change in tumor burden. There were concordant changes in sialic acid in 95%, and in 85%, these were considered significant. For patients responding to treatment, reduction in tumor burden was relatively rapid, providing no effective lead time between change in sialic acid and other evidence of clinical improvement. Of the progressing patients with significant changes in sialic acid, 85% demonstrated a lead time of 1 to 21 wk. Although suggested by others as a clinical marker, in this study, carcinoembryonic antigen did not correlate with tumor burden. However, we did find a significant correlation between sialic acid and tumor burden, and the results of serial studies suggested that this may be clinically valuable in guiding patient management. (Author abstract) (7 Refs)

30. CEA LEVELS IN THE PERITONEAL FLUID OR WASHINGS OF PATIENTS WITH OVARIAN NEOPLASMS (MEETING ABSTRACT).

Turrin A, Buraggi GL, BombardieriE, Ringhini R, Spinelli P, Stefanon B, Pilotti S, De Palo G
Istituto Nazionale per lo Studio e la Cura dei Tumori, Milan, Italy
Tumori; 67(2,SupplA):115 1981

The level of ip carcinoembryonic antigen (CEA) (peritoneal fluid or peritoneal lavage) was determined in 172 patients of who 112 had ovarian carcinoma (58 without and 54 with peritoneal invasions) and 60 had benign tumor of the ovary or nonneoplastic diseases of the uterus or liver. Peritoneal fluid was present in 29 patients, and peritoneal lavage was performed in 143. Av ip CEA values (ng/ml) for the paients in question are reported. The data show clinical significance for ip CEA in mucinous carcinoma. For the other histological types there is good correlation between CEA positivity and peritoneal involvement by disease only when ascitic effusions are present. (no Refs) (In ITA)

31. MALIGNANT GERM CELL TUMORS OF THE OVARY; CLINICOPATHOLOGICAL STUDY.

Ishige H, Nagao K, Kuwahara T, Ueno T, Maruyama K, Suzuki M, Shoogimen M, Yoshiwara T
Dept. Pathology, Chiba Cancer Center Res. Inst., Nitona-cho, Chiba 280, Japan
Chiba Med J; 57(1):19-28 1981

During the period from 1973 to 1979, eight patients (including four unmarried women) with malignant germ cell tumor of the ovary were treated at our clinic. By the WHO classification, these cases included one case of embryonal carcinoma, one case of dysgerminoma, two cases of endodermal sinus tumor, one case of teratoma mixed with choriocarcinoma. one case of teratoma mixed with endodermal sinus tumor and two cases of dysgerminoma mixed with endodermal sinus tumor. Clinicopathological findings of these patients were reviewed in association with the serum level of 'tumor products' including alpha-fetroprotein (AFP), human chorionic gonadotropin (HCG), carcinoembryonic antigen and lactic dehydrogenase (LDH). The age range was 15 to 43 yr (av 28 yr). The serum level of AFP was elevated in all patients with endodermal sinus tumor. The serum level of HCG was elevated in only one case of choriocarcinoma mixed with teratoma in which HCG was identified by the immunoperoxidase technique in choriocarcinoma cells. The serum level of LDH was elevated in all patients with lethal tumors. The measurement of the serum level of specific tumor products was helpful in determining the extension and recurrence of the tumors and prognosis of patients. While lymph node metastasis was seen in one case of embryonal carcinoma and visceral organ metastasis was seen in two cases of teratoma mixed with choriocarcinoma, and embryonal carcinoma, peritoneal carcinomatosis was seen in all patients, indicating the rapid growth rate of these tumors. (22 Refs) (In JPN)

32. THE ENDOCRINOLOGY OF TESTICULAR GERMINAL CELL TUMOURS.

Aiginger P, Kolbe H, Kuhbock J, Spona J, Geyer G
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Acta Endocrinol (Copenh); 97(3):419-426 1981

Estradiol (E2), testosterone (T), luteinizing hormone (LH), follicle stimulating hormone (FSH), beta-human chorionic gonadotropin (beta-hCG) and alpha-1 fetoprotein (AFP) were measured in blood samples taken from 63 patients with testicular tumors. In patients without tumor recurrence (n = 31) AFP, E2 and T were within the normal range, beta-hCG was negative, LH levels were marginally elevated and FSH concentrations were significantly elevated. In patients with tumor recurrence (n = 32) E2 was significantly elevated, whereas the T levels varied considerably and were therefore statistically not different from the patients without tumor recurrence. The beta-hCG positive subgroup of the recurrence group, however, demonstrated significantly elevated T levels. T levels were highest in patients with 51 to 500 U beta-hCG/l. On the other hand T was normal or even low normal in beta-hCG negative-AFP positive patients. In all subgroups decreasing FSH levels and decreasing LH responses to LRH were among the earliest signs of tumor recurrence. The observations suggest that moderate hCG levels are able to stimulate testicular T production, whereas high levels no longer increase T serum concentrations. Increased conversion rates from steroid precursors to estradiol seem to be a feature of beta-hCG positive as well as beta-hCG negative testicular tumors. (Author abstract) (20 Refs)

33. CLINICAL EVALUATION OF HUMAN CHORIONIC GONADOTROPIN (HCG), ALPHA-FETOPROTEIN (AFP), PROSTATIC SERUM ACID PHOSPHATASE (PSAP), CARCINOEMBRYONIC ANTIGEN (CEA) AND BETA-2-MICROGLOBULIN (B2MG) AS TUMOR MARKERS IN UROGENITAL MALIGNANCIES.

Kawamura J, Soeda A, Okada K, Yoshida O, Kosaka T, Nakajima K, Yoshi M, Morita R, Torizuka K
Dept. Urology, Faculty Medicine, Kyoto Univ., Kyoto, Japan
Hinyokika Kiyo; 27(3):269-278 1981

Serum hCG and AFP for testicular germ cell tumors, prostatic serum acid phosphatase (PSAP) for prostatic carcinoma, and serum CEA and B2MG for urogenital malignancies were measured by radioimmunoassay (RIA) techniques. A. Specific tumor marker: 1) hCG and AFP: AFP was detected in embryonal carcinoma (EC), infantile EC and teratocarcinoma (TC). AFP and/or hCG was detected in the mixed type of tumor consisting of EC, TC and choriocarcinoma. This was dependent on the major histological component of the tumor. Even in the pure seminoma, elevation of hCG was noted in 4 out of 17 cases, followed by normalization after orchiectomy. Alteration of AFP and hCG well demonstrated an effect of treatment and clinical courses. Reelevation of the markers revealed an advance of clinical staging and recurrence of the tumor. 2) PSAP: Serum levels of PSAP by RIA method correlated well with those by enzyme method but showed fewer pseudonegative values. Elevation of PSAP gave a clue to the initial diagnosis and to earlier detection of recurrence of prostatic carcinoma. B. Nonspecific tumor marker: 1) B2MG: Elevation of B2MG was seen in patients with advanced stage of urogenital malignancies. Such a rate of elevation was 62.5% in testicular carcinoma, 55.6% in renal cell carcinoma, 48.1% in bladder carcinoma, 45.5% in pelvic and ureteral tumors and 22.2% in prostatic carcinoma. B2MG increased in 46.9% of advanced urogenital cancers as a whole. 2) CEA: CEA was also elevated in the advanced stage of urogenital cancers, although its percentage was less than that in B2MG. Elevation of CEA was detected in 44.4% of prostatic carcinomas, 37.0% of bladder carcinomas, 36.4% of pelvic and ureteral tumors and 22.2% of renal cell carcinomas. No testicular carcinomas revealed an abnormal CEA value. 3) Combination of B2MG and/or CEA did not raise positive rates of the markers in each of the urogenital cancers. However, when these patients were divided into three groups such as 'alive' with disease and 'dead', according to the survival states, elevation of B2MG or B2MG and CEA was seen in patients in whom tumorous lesions were not eliminated or recurrence was noticed, indicating a poor prognosis. In conclusion, to estimate AFP and hCG or PSAP, as a specific tumor marker, and B2MG and/or CEA, as a nonspecific tumor marker, is a useful adjunct to detect clinical courses and to predict prognosis of urogenital malignancies. (28 Refs) (In JPN)

34. CARCINOEMBRYONIC ANTIGEN (CEA) IN PATIENTS WITH UROLOGIC CANCER. II. THE CLINICAL UTILITY OF PLASMA CEA AND URINARY CEA-LIKE SUBSTANCE IN UROTHELIAL CANCER.

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Hinyokika Kiyo; 27(3):231-241 1981

Determinations were made of plasma CEA in 124 bladder cancer and 26 renal pelvic and ureteral cancer patients and also of urinary CEA in 86 bladder cancer patients by radioimmunoassay (zirconylphosphate-gel) with the following results. 1)Plasma CEA levels (mean +- SD) thus found were 2.4 +-1.6 ng/ml for normal subjects and 3.0 +-1.9 ng/ml for patients with benign urologic diseases. Patients with localized bladder cancer and those with metastasis gave respective values of 5.7 +-3.9 ng/ml and 10.7 +-8.1 ng/ml, which were significantly higher than a corresponding value for those with previous history of bladder cancer of 3.1 +-1.8 ng/ml (p less than 0.01). Of patients with renal pelvic and ureteral cancer, those with localized lesions gave a value of 6.0 +-6.0 ng/ml and those with metastasis showed a value of 13.8 +-9.9 ng/ml, the latter value being significantly higher than a corresponding value for those with previous history of renal pelvic and ureteral cancer of 3.6 +-2.4 ng/ml (p less than 0.05). 2) If cases showing plasma CEA levels of 6 ng/ml or above are regarded as CEA-positive, the positivity rates of plasma CEA in bladder cancer patients were 40.8% for the group with localized cancer and 67% for the group with metastasis; both figures were significantly higher than that for the group with previous history of bladder cancer, 7.6% (p less than 0.01). Among patients with renal pelvic and ureteral cancer, 38.5% of those with localized cancer and 71.4% of those with metastasis were positive for plasma CEA, with the latter figure being found to be significantly higher than a corresponding value for patients with previous history of renal pelvic and ureteral cancer of 16.7% (p less than 0.05). 3) Fifty-four bladder cancer patients who were followed up for more than 6 mo after operation were divided into two groups, with and without recurrence, and plasma CEA levels as determined before and 1 mo after operation were compared between the two groups. 4)Plasma CEA levels were further studied in relation to smoking habits. Urothelial cancer patients, regardless of whether smokers or nonsmokers, showed a significantly higher positivity rate of plasma CEA than benign disease patients (p less than 0.01). 5)Urinary CEA levels tended to be higher in females than in males. Even benign disease patients exhibited abnormally elevated urinary CEA levels in the presence of urinary tract infection, with a positivity rate in excess of 60%. 6) These results suggest that the plasma CEA as determined by immunoassay provides a useful means of assessing the efficacy of surgical treatment, determining the likelihood of recurrence and the presence or absence of metastasis and evaluating prognosis in patients with urothelial cancer. (23 Refs) (In JPN)

35. CARCINOEMBRYONIC ANTIGEN AND ALBUMIN CONCENTRATIONS IN BRONCHOALVEOLAR LAVAGE FLUID (MEETING ABSTRACT).

Lemarie E, Lavandier M, Gauthier F, Lebreton de Vonne T, Frappe N, Renoux M, Renoux G
Centre Hospitalier Universitaire Bretonneau, 37044 Tours Cedex, France
Am Rev Resp Dis; 123(4,Part2):65 1981

We studied the levels of carcinoembryonic antigen (CEA) and albumin (ALB) in the bronchoalveolar lavage (BAL) fluid of 27 subjects. 9 were normal, healthy, volunteers. 10 patients were affected with endothoracic sarcoidosis and 8 with bronchogenic carcinoma. CEA and ALB level were determined in the 3 successive samples of BAL fluid recovered after 3 intrapulmonary injections of 50 ml of isotonic saline. As a mean, 26 ml were recovered after each saline administration. Under such conditions, covariance analysis of the results evidences that the amount, in ng per ml, of CEA is not dependent upon the number of sampling, whatever might have been the clinical diagnosis. However, we found a significant correlation between the CEA concentration and the vol of fluid recovered. Similar results were observed in regards of ALB concentrations. In spite of variations occurring in the same way, there was no association between the amount of CEA and that of ALB. High levels of CEA (cancer patients) were found in BAL with low ALB concentrations. In addition, there was a significant correlation between the concentration of CEA per ml and the total quantity of CEA in the total BAL samples. These data suggest that the variation of the apparent concentration of either CEA or ALB depends upon the vol of BAL recovered, even if pulmonary diseases such as lung cancer or local inflamation can increase CEA or ALB respectively. As a practical procedure, it appears that the sample recovered after pulmonary injection of 50 ml saline is sufficient for a presumptive diagnosis of lung cancer by CEA titration. (no Refs)

36. CARCINOEMBRYONIC ANTIGEN IN RETINOBLASTOMA (MEETING ABSTRACT).

Minoda K, Komatsu M, Kojima T
Department of Ophthalmology, Tokyo University Branch Hospital, Tokyo, Japan
International Symposium on Intraocular Tumors, May 17-20, 1981, Schwerin, W Germany European Ophthalmology Society; :A49 1981

Plasma carcinoembryonic antigen (CEA) and alpha fetoprotein (AFP) were studied in 74 children with retinoblastoma, 5 cases of leukokoria, and 14 normal controls. In 24 cases of retinoblastoma (8 unilateral, 16 bilateral) CEA and AFP titles were investigated before and after enucleation of their unilateral eyes. The CEA title before enucleation was significantly higher than that of the controls and it was significantly lowered after enucleation. On the other hand, the AFP title was not significantly different from that of the controls. In 36 cases of bilateral retinoblastoma, CEA and AFP titles were examined after conservative treatment and their titles were not significantly different from those of the controls. In 5 cases of leukokoria, none of them showed abnormal titles of CEA or AFP. (no Refs)

ULTRASTRUCTURE/ CYTOCHEMISTRY

37. MALIGNANT GERM CELL TUMOR OF THE PINEAL REGION - IMMUNOHISTOCHEMICAL STUDY OF AFP AND HCG.

Kimura N, Namiki T, Wada T
Dept. Pathology, Natl. Hosp. of Sendai, Sendai, Japan
Gan No Rinsho; 27(9):1135-1140 1981

Levels of serum and tissue alpha-fetoprotein (AFP) and human chorionic gonadotropin (hCG) were determined in a 17-yr-old man with acute onset of symptoms of pineal gland tumor (endodermal s inus tumor) and in a 25-yr-old man with 6-mo duration of symptoms due to a pineal gland tumor (choriocarcinoma). The 17-yr-old patient was diagnosed on the basis of abnormal serum AFP levels (161,583.0 nanog/ml); this patient had normal serum hCG and luteinizing hormone levels. At autopsy, histological examination indicated that most of the tumor cells in the endodermal sinus tumor showed localized AFP; further study also showed that there were ip tumor implantations via a ventriculo-peritoneal shunt, metastases to mesenteric lymph nodes, and tumor cells in ascites. In case 2, a typical choriocarcinoma that was composed of syncytiotrophoblasts and cytotrophoblasts was observed; only the syncytiotrophoblastic cells were observed to contain hCG. (21 Refs) (In JPN)

38. CLINICAL STUDIES OF CARCINOEMBRYONIC ANTIGEN (CEA) IN TUMOR TISSUE AS A PARAMETER FOR DETERMINING THE PROGNOSIS OF COLON CANCER; COMPARISON OF HISTOLOGICAL STAGE AND CEA VALUE IN THE BLOOD (MEETING ABSTRACT).

Hamada Y, Yamamura M, Koyama H, Takada H, Hioki K, Yamamoto M
Dept. Surgery, Kansai Medical Univ., Moriguchi-shi, Osaka Pref. 570, Japan
Nippon Geka Gakkai Zasshi; 82(Suppl):172 1981

CEA staining by the enzyme antibody method was performed on 16 colon cancers and 40 rectal cancers. Eleven well differentiated adenocarcinomas and 36 moderately differentiated adenocarcinomas were classified according to their CEA staining ability: localized staining type (Grade I), tubular secretion type (Grade II) and interstitial infiltration type (Grade III). Histologically, all 49 adenocarcinomas, 2 mucinous carcinomas and 2 signet ring cell carcinomas were positive for CEA, and 3 squamous cell carcinomas and 1 malignant lymphoma were negative, giving a positive CEA staining rate of 92.8%. According to Duke's classification, the positive rate of CEA in the blood was 30%, 58% and 84% for A, B and C types, respectively, which reflected the stage of cancer. The CEA positive rate in the blood was 16.7%, 70.3% and 100% for grades I, II and III, respectively. The grade was advanced in moderately differentiated adenocarcinoma and in adenocarcinoma invading into the proper muscle and beyond. Lymph node metastasis was found in 0%, 48% and 100% of grades I, II and III, respectively. However, lymphatic invasion and max tumor diameter were not related to the grade. This graded classification of CEA in tumor tissue was considered to be a good parameter for foreseeing and determining the clinical stage of colon cancer. (no Refs) (In JPN)

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ONCOFETAL PROTEINS

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STRUCTURE/ IDENTIFICATION/ CHARACTERIZATION

1. A PANCREATIC ONCOFETAL ANTIGEN: ITS PARTIAL PURIFICATION AND CLINICAL APPLICATION.

Homma T, Oguchi H, Kawa S
Second Dept. Internal Medicine, Shinshu Univ. Sch. Medicine, Asahi 3-1-1, Matsumoto, 390, Japan
Gastroenterol Jpn; 16(3):268-274 1981

Studies on the purification, characterization and clinical application of pancreatic oncofetal antigen were reported. This antigen was purified from fetal pancreas, and migrated in the beta-region on electrophoresis. Its mol wt was about 80 x 10(4) daltons on gel filtration with a Sephacryl S-300. This antigen is clearly different from other oncofetal antigens such as alphafetoprotein, carcinoembryonic antigen or ferritin. Clinically, this pancreatic oncofetal antigen was positive in sera of 68.4% of the patients with pancreatic cancer. However, an elevated level of this antigen was also observed in the sera of some patients with biliary tract cancer, colon cancer or gastric cancer. The antigen was also found in pancreatic juice obtained from patients with pancreatic cancer in almost the same incidence as

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in their sera. It is suggested that a pancreatic oncofetal antigen assay of sera and pancreatic juice in combination with other oncofetal antigens is valuable for the diagnosis and monitoring of the clinical course of pancreatic cancer. (Author abstract) (15 Refs)

ASSAY PROCEDURES/ SYNTHESIS

2. EVALUATION OF A COMMERCIAL ENZYME IMMUNOASSAY KIT FOR SERUM CARCINOEMBRYONIC ANTIGEN.

Fabricatorian D, Gallagher ND

A. W. Morrow Dept. Gastroenterology, Royal Prince Alfred Hosp., Missenden Rd., Camperdown, NSW 2050, Australia

Ann Clin Biochem; 18(part4):248-251 1981

The Abbott CEA-EIA Diagnostic enzyme immunoassay kit for measuring serum carcinoembryonic antigen (CEA) is evaluated and compared to the Roche-CEA Z-Gel radioimmunoassay kit. incubated with extraction buffer and then centrifuged. The supernatant is placed in tray wells. Plastic beads coated with guinea-pig anti-CEA are added as first antibody. The beads are washed. Goat anti-CEA conjugataed with horse radish peroxidase is then added as the second antibody. The beads are again washed, placed in a buffer and incubated. After the reaction is stopped, absorption is measured at 492 nanometer. Results indicate that the method has good reproducibility and no problem with drift in standard values. The cut-off point for elevated CEA is 2.5 nanog/ml. The method tested eliminates the need for labor-intensive dialysis necessary in the other method. A highly-skilled technician is not needed. The kit appears to be an accurate and cheap alternative to other test kits. (14 Refs)

3. SOLID-PHASE RADIOIMMUNOASSAY OF CEA BY AN ANTISERUM NONCROSSREACTIVE WITH FECAL ANTIGEN AND ITS CLINICAL REULTS.

Tamada R

Second Dept. Surgery, Faculty Medicine, Kyushu Univ., Fukuoka 812, Japan

Fukuoka Igaku Zasshi; 72(6):350-367 1981

A solid-phase radioimmunoassay system for detecting circulating carcinoembryonic antigen (CEA) in patients with digestive tract cancer is described. The system uses a polystyrene tube and was developed with purified CEA from liver metastases of colon cancer and highly absorbed rabbit anti-CEA serum. Preoperative serum CEA levels in 50/127 cancer patients were higher than those of healthy persons; 70% of colorectal cancer, 53% of gastric cancer, 27% of breast cancer, and 19% of esophageal cancer patients were positive for CEA. The solid-phase radioimmunoassay showed more specificity for colorectal cancer (p less than 0.005) than Roche's radioimmunoassay, but there was no significant difference for gastric or other cancers. Detection of colorectal cancer is facilitated because the radioimmunoassay does not detect fe cal antigen. (55 Refs) (In JPN)

4. HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY QUANTITATION OF N-ACETYLNEURAMINIC ACID IN MALIGNANT MELANOMA AND BREAST CARCINOMA.

Silver HK, Karim KA, Gray MJ, Salinas FA

Cancer Control Agency British Columbia, 2656 Heather St., Vancer, B.C. V5Z 3J3, Canada

J Chromatogr; 224(3):381-388 1981

A rapid isocratic high-performance liquid chromatography (HPLC) method for quantitation of serum N-acetylneuraminic acid (NANA) is described. Separation is achieved on an Aminex HPX-87 cation-exchange resin using a 0.006 N sulfuric acid mobile phase. Compared with the more conventional thiobarbituric acid (TBA) method, HPLC is more reliable and has a much improved max sensitivity of 0.8 nmol/ml. In a limited study of malignant melanoma patients' sera, HPLC gave slightly higher values for NANA than TBA. In a more detailed study of breast carcinoma patients with measurable tumor burden, HPLC and TBA methods were used on the same sera and compared with concurrent carcinoembryonic antigen (CEA) determinations. HPLC resulted in a clear improvement in discrimination between tumor burden groups compared with either the TBA method or CEA. (Author abstract) (35 Refs)

EXPERIMENTS IN ANIMAL SYSTEMS

5. EFFECTS OF CIS-PLATINUM DIAMMINE DICHLORIDE ON YOLK SAC TUMOR TRANSPLANTED IN NUDE MICE.

Sawada M, Matsui Y, Nishiura H, Yagyu M, Hayakawa K, Okudaira Y, Kawashima M, Iwanaga K

Dept. Gynecology, Res. Inst. Microbial Diseases, Osaka Univ., Suita-shi, Osaka Pref. 565, Japan

Nippon Sanka Fujinka Gakkai Zasshi; 33(4):519-524 1981

The effects of a new anticancer drug cis-platinum diammine dichloride (CPDD) on yolk sac tumors were studied. Human yolk sac tumor serially transplanted in BALB/c nude mice (YST-1) was used as material in this experiment. Two methods of administration of CPDD were examined and compared: (1) CPDD 5 mg/kg x 1 day x 4 and (2) CPDD 1 mg/kg x 5 days x 4. Tumor size was measured and serum alpha-fetoprotein (AFP) of nude mice was determined by radioimmunoassay during experiments. At the end of the experiments, the treated tumor was resected and examined by light and electron microscopy. The results were as follows: CPDD was active in regressing yolk sac tumor at doses of 5 mg/kg given as a single treatment and doses of 1 mg/kg given daily for 5 days. It appeared that CPDD showed higher activity against tumors by daily injections at doses of 1 mg/kg. Close correlation was recognized between tumor size and serum AFP of nude mice (r = 0.93, p less than 0.001). Serum AFP of tumor-bearing nude mice was revealed to be a useful marker of yolk sac tumor in nude mice as in the human patient. The effect of CPDD on tumor cells was confirmed by light and electron microscopy. (11 Refs) (In JPN)

6. IN VIVO REGULATION OF OVARIAN ACTIVITY BY ALPHA-FETOPROTEIN.

Aussel C, Lafaurie M, Masseyeff R, Stora C
Faculte de Medicine, Inserm U210, Chemin de Vallombrose, 06034 Nice Cedex, France
Steroids; 38(2):195-204 1981

Adult female rats, each injected with 760 ug alpha-fetoprotein (AFP) weekly, presented after the 3rd wk a decrease of ovarian activity evidenced by a decreased number of maturing follicles, corpora lutea, and a drop in ovarian wt. The level of progesterone was low and agreed with the deceased number of corpora lutea. Conversely, total and free estradiol-17beta levels remained normal despite the known ability of AFP to bind estrogenic hormones. A regulatory role of AFP during the postnatal stage of sexual maturation is proposed. (Author abstract) (27 Refs)

7. PRESENCE OF ANTI-GAMMA-FA-REACTIVE ANTIGENS IN SPONTANEOUS AND CARCINOGEN-INDUCED MALIGNANCIES OF EXPERIMENTAL ANIMALS.

Higgins PJ, Tong C, Borenfreund E
Lab. Cell Biochemistry, Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
Oncology; 38(6):340-345 1981

Immunochemical analysis of various tumors, representing 12 different tissue sites of origin, revealed a gamma-fetal antigen(gamma-FA)-like component in 17 of 23 malignant neoplasms of the mouse. This antigen was identified in extracts of spontaneous and carcinogen-induced murine tumors as well as in extracts of hepatic tumors initiated in the rat with diethylnitrosamine. The occurrence of gamma-FA in 75% of the malignant tumors examined and its presence in the sera of rodents bearing transplanted and primary cancers suggests an associative relationship of potential diagnostic value. This possibility is supported by the observation that immunoprecipitable gamma-FA appeared in the sera of hepatocarcinogen-treated rats several wk prior to the detection of alpha-fetoprotein. (Author abstract) (26 Refs)

IMMUNOLOGIC INTERACTIONS

8. IN VITRO PRODUCTION OF HUMAN ANTIBODY TO A TUMOUR-ASSOCIATED FOETAL ANTIGEN.

Irie RF, Jones PC, Morton DL, Sidell N
Div. Oncology, Univ. California Sch. Medicine, 54-140 CHS, Los Angeles, CA, 90024
Br J Cancer; 44(2):262-266 1981

After the establishment of lymphoblastoid cell lines that synthesize antibody directed against a human tumor-associated fetal antigen designated as oncofetal antigen-I (OFA-I), a method is described for the production of IgM anti-OFA-I in vitro. Ten serum samples containing high levels of anti-OFA-I were identified and viably frozen peripheral-blood lymphocytes (PBL) from the same patients were transformed by Epstein-Barr virus (EBV). Patients included five given adjuvant immunotherapy with an OFA-I+ tumor-cell vaccine (TCV), three treated with BCG, and two treated only by surgical excision. Anti-OFA-I levels in the spent medium were monitored by immune-adherence using the OFA-I+ melanoma cell line UCLA-SO-M 14 (M14), as the target cell. Two of the EBV-infected cultures (ES from the TCV group and CD from the surgery only group) produced detectable antibody to M14 cells by day 6. By day 9, culture DV (BCG group) became positive. The CD culture was positive only for 9 days, while ES (obtained from the patient with the highest anti-OFA-I titer) ceased growth after 3 wk. The supernatants displayed no reactivity against a control lymphoblastoid cell line autologous to the M14 donor. The DV lymphoblasts continued to produce increasing titers of anti-M-14 antibody until day 42, with gradual decrease by day 60 and became negative on day 66. None of the other 7 PBL cultures became positive to M14. Further studies determined that the antibody exhibited specific reactivity to an antigen associated with human cancer. No antibody reactivity in the DV culture medium was detected to a number of target cells tested. Assessment of the immunoglobulin class indicated the anti-OFA-I was limited to the IgM class. The DV spent medium was cytotoxic in the presence of either rabbit or human complement. (21 Refs)

CLINICAL/ DIAGNOSIS/ IMMUNOTHERAPY

9. LOCALISATION OF MALIGNANT GERM-CELL TUMOURS BY EXTERNAL SCANNING AFTER INJECTION OF RADIOLABELLED ANTI-ALPHA-FETOPROTEIN.

Halsall AK, Fairweather DS, Bradwell AR, Blackburn JC, Dykes PW, Howell A, Reeder A, Hine KR
(c/o Fairweather) Immunodiagnostic Res. Lab., Dept. Immunology, Univ. Birmingham Medical Sch., Birmingham B15 2TJ, England
Br Med J; 283(6297):942-944 1981

Sheep IgG antibody to alpha-fetoprotein was labeled with 131I and used to identify human germ-cell tumors by emission scanning. Eleven patients were studied after resection of their primary tumors. Ten had malignant teratoma and 1 an endodermal sinus tumor. All eight patients with raised serum alpha-fetoprotein concentrations had metastases apparent in the antibody scans. Of the remaining three patients with normal serum alpha-fetoprotein concentrations, two had positive scans. Three of the patients with positive results were scanned twice; the second scans were negative after treatment, when the alpha-fetoprotein concentrations had returned to normal. These results suggest that antibody scans are useful in the clinical management of patients with germ-cell tumors. (Author abstract) (12 Refs)

10. BIOLOGIC MARKERS IN CANCER DIAGNOSIS AND TREATMENT.

Holyoke ED, Block GE, Jensen E, Sizemore GW, Heath H, Chu TM, Murphy GP, Mittelman A, Ruddon RW, Arnott MS
Roswell Park Memorial Inst., Buffalo, NY
Curr Probl Cancer; 6(2):68pp. 1981

The clinical use of tumor markers in detecting and monitoring the progress of tumor treatment is reviewed. In breast cancer treatment, the intracellular presence of an estrogen receptor protein identifies those tumors that are hormone-dependent and thus capable of responding to hormone manipulatio n (therapy). The presence or absence of progesterone receptors has not proved clinically useful. Calcitonin has been shown to be useful as a biological marker of medullary thyroid carcinoma; there are numerous tests and measurements for it, such as pentagastrin injection, long calcium infusion, short calcium infusion, and ethanol ingestion. The measurement of elevated levels of prostatic acid phosphatase by such techniques as radioimmunoassay, counterimmunoelectrophoresis, solid-phase immunofluoroassay, and solid-phase immunoadsorbent assay offers a method of identifying patients in the early stages of prostate cancer and monitoring the efficacy of treatment. The detection of certain 'tumor-associated antigens' such as alpha-fetoprotein, tissue peptide antigen, fetosulfoglycoprotein, pancreatic oncofetal antigen, and carcinoembryonic antigen (CEA) have various applications in screening, diagnosis, and staging of cancer; CEA may be of value in monitoring the adequacy of therapy and the treatment of advanced disease and in detecting persistent progressive disease in patients with colon cancer; alpha-fetoprotein is sensitive and specific enough for hepatocellular cancer to be of clinical use in this disease. Various protein degradation products are associated with tumors; plasminogen-dependent protease activity is one of the most likely candidates for a proteolytic activity as a tumor marker substance. Measurements of plasminogen activator, plasmin-derived products, and plasma protein degradation products in serum and/or urine are being investigated for their utility as tumor markers. Measurements of tissue aryl hydrocarbon hydroxylase may help to identify populations at risk of cancer resulting from chemical carcinogenesis. (245 Refs)

11. USE OF IMMUNOLOGICAL TESTS FOR PROGNOSIS OF CANCER OF THE STOMACH.

Blokhina NG, Sinitsyn VA, Kadagidze ZG, Tkacheva GA
All-Union Cancer Res. Center, Moscow, USSR
Vestn Akad Med Nauk SSSR; (7):44-49 1981

The prognostic value of immunological indices was studied in 196 patients with cancer of the stomach. Prior to the surgery, the patients with cancer of the stomach had markedly elevated concentration of the carcinoembryonic antigen (CEA: 65.9 nanog/ml, compared with 13.3 nanog/ml in the patients with benign stomach lesions and 5.2 nanog/ml in healthy controls), significantly decreased B-lymphocyte count (7.2% vs 10.6% and 14.7%), IgA and IgG content, and significantly increased number of negative skin reactions to 2,4-dinitrochlorobenzene and tuberculin. The degree of immunodepression depended upon the extent of infiltration of the stomach wall: the most pronounced inhibition of immune response and the highest CEA levels were recorded in the patients with endophytic tumors. Postoperative normalization of CEA concentration and the indices of skin tests was indicative of recurrent-free course of the dis ease. (4 Refs) (In RUS)

12. STUDIES INTO CARCINO-EMBRYONIC ANTIGEN (CEA) AND ENZYME ACTIVITIES OF ALKALINE AND ACID PHOSPHATASE IN PATIENTS WITH FIBROCYSTIC BREAST DISEASE.

Opri F, Kirchner H
Frauenklinik und -poliklinik, Freien Universitat Berlin im Klinikum Steglitz, Hindenburgdamm 30, D-1000 Berlin (West) 45, W. Germany
Zentralbl Gynaekol; 103(10):564-568 1981

CEA as well as alkaline and acid phosphatase were measured in patients with fibrocystic breast disease. The values recorded from the punctured fluids were compared to those in peripheral blood. CEA concentrations in cyst fluid were elevated in patients with proliferative breast disease, whereas no correlations could be established between alkaline and acid phosphatase, on the one hand, and various histological forms of breast disease, on the other. (Author abstract) (20 Refs) (In GER)

13. CARCINOEMBRYONIC ANTIGEN ESTIMATION IN CEREBROSPINAL FLUID IN PATIENTS WITH METASTATIC BREAST CANCER.

Dearnaley DP
Ludwig Inst. for Cancer Res. (London Branch), Royal Marsden Hosp., Sutton, Surrey, England
Oncodev Biol Med; 2(4):305-311 1981

The value of measuring cerebrospinal fluid (CSF) levels of carcinoembryonic antigen (CEA) as a guide in the differential diagnosis of patients with breast cancer and neurologic symptoms was examined in 39 patients with metastatic breast carcinoma (22 of whom had metastases to the CNS) and 13 control patients with various benign neurological disorders. None of the control patients had any detectable CSF CEA. There was no correlation between CEA levels in simultaneously obtained plasma and CSF samples in the patients with metastatic breast cancer. Immunoreactive CSF CEA was found in 13/22 patients with breast cancer metastases involving the CNS and in 4/17 without CNS involvement. A similar range of values of CSF CEA was found in patients with meningeal infiltration, extra-dural spinal metastases, or without CNS involvement, showing that the degree of elevation of CSF CEA is not helpful in determining the site or presence of CNS involvement in patients with metastatic breast cancer. (12 Refs)

14. SIGNIFICANCE OF SERUM CONCENTRATIONS OF CARCINOEMBRYONIC ANTIGEN, FERRITIN, AND CALCITONIN IN BREAST CANCER.

Bezwoda W, Derman D, Bothwell T, MacPhil P, Levin J, De Moor N
Dept. Medicine, Medical Sch., Hospital St., Johannesburg, S. Africa
Cancer; 48(7):1623-1628 1981

Serum concentrations of carcinoembryonic antigen (CEA), ferritin, and calcitonin were measured in 107 patients with breast cancer, 80 of whom had overt or occult metastatic disease. CEA and ferritin values were statistically higher in those patients with metastases. In contrast, there was no correlation between calcitonin concentrations and the stage of the disease. All 27 subjects with CEA concentrations greater than 80 ug/liter and 32 of 40 with values between 41-80 ug/liter had metastatic disease. Ferritin was a definite but less sensitive discriminator, with metastatic disease present in all nine patients having concentrations greater than 400 ug/liter. Such metastases were invariably hepatic. When the two measurements were used as a combined discriminant, the diagnostic accuracy increased somewhat. All 32 patients with a CEA concentration greater than ug/liter and/or a ferritin concentration greater than 400 ug/liter had metastatic disease; the same was true for 32 of the 42 subjects with CEA concentration between 41-80 ug/liter and/or a ferritin concentration between 200-400 ug/liter. The measurements and prognostic value, both when assessed alone and together, with a median survival from the time of study significantly shorter in those with the highest values. (Author abstract) (23 Refs)

15. MULTIPLE BIOLOGIC MARKERS IN THE MONITORING OF TREATMENT FOR PATIENTS WITH SMALL CELL CARCINOMA OF THE LUNG: THE USE OF SERIAL LEVELS OF PLASMA CEA AND SERUM CARBOHYDRATES.

Woo KB, Waalkes P, Abeloff MD, Ettinger DS, McNitt KL, Gehrke CW
Johns Hopkins Oncology Center, 600 North Wolfe St., Baltimore, MD, 21205
Cancer; 48(7):1633-1642 1981

The monitoring utility of serial patterns of a single marker (carcinoembryonic antigen) level and multiple marker (three carbohydrates-fucose, mannose and galactose) levels in patients with small cell carcinoma of the lung was investigated using a quantitative approach. A serial multiple regression (SMR) model was formulated to assess the disease responses following the 1st to the 10th course of therapy and resulted in the multiple correlations ranging from 0.183 (NS)-0.706 (p less than 0.005) for CEA, and 0.502 (p less than 0.250)-0.760 (p less than 0.025) for three carbohydrates, respectively. The appraisal of these markers utilizing the SMR model points out that: (1) the serial levels of CEA greater than 5.0 ng/ml are significantly correlated with the disease course whereas the serial levels less than 5.0 ng/ml reflect the trend of variation in the disease course, but with less accuracy; and (2) the levels of three carbohydrates, any one elevated before and during therapy, are significantly correlated with the disease course. (Author abstract) (31 Refs)

16. ALPHA FETOPROTEIN DETERMINATIONS IN THE MANAGEMENT OF ENDODERMAL SINUS TUMORS AND MIXED GERM CELL TUMORS OF THE OVARY.

Romero R, Schwartz PE
(c/o Schwartz) Dept. Obstetrics and Gynecology, Yale Univ. Sch. Medicine, 333 Cedar St., P.O. Box 3333, New Haven, CT, 06510
Am J Obstet Gynecol; 141(2):126-131 1981

Serum alpha fetoprotein (AFP) titers determined by radioimmunoassay (RIA) techniques may serve as useful tumor markers in patients with endodermal sinus tumors (EST) or mixed germ cell tumors of the ovary containing EST elements when serum AFP is detectable prior to initiation of combination chemotherapy. A decline in AFP titers to less than 20 ng/ml, followed by any subsequent elevation, is an ominous finding suggestive of recurrent or progressive disease and requires prompt diagnostic evaluation and change in management. AFP assays performed by non-RIA techniques lack sufficient sensitivity to be employed routinely as tumor markers. (Author abstract) (16 Refs)

ULTRASTRUCTURE/ CYTOCHEMISTRY

17. CARCINOEMBRYONIC ANTIGEN AND PROGNOSIS AFTER RADICAL SURGERY FOR LUNG CANCER: IMMUNOCYTOCHEMICAL LOCALIZATION AND SERUM LEVELS.

Ford CH, Stokes HJ, Newman CE
Surgical Immunology Unit, Clinical Oncology, Univ. Birmingham, Queen Elizabeth Hosp., Edgbaston, Birmingham B15 2TH, England
Br J Cancer; 44(2):145-153 1981

Eighty-two percent of tumor sections from 105 patients with lung cancer showed positive immunocytochemical localization of an anti-carcinoembryonic antigen (CEA) Ig free of antibody to normal cross-reacting antigen (NCA). The highest incidence was found in adenocarcinomas, and no association between staining and disease stage was found. There was a relationship between positive-staining tumors and preoperative and postoperative serum CEA levels of greater than or equal to 20 ng/ml, but the high incidence of CEA+, less than 20 ng/ml serum patients indicated that immunocytochemical localization was of little value in selecting patients for sequential serum monitoring. Staining for CEA was not prognostic but a preoperative serum CEA level greater than or equal to 20 ng/ml was associated with a poor prognosis in patients undergoing radical surgery for lung cancer (p = 0.043). This prognostic effect of CEA was seen mainly in patients whose tumors showed the greatest immunocytochemical localization (p = 0.017) and in Stage III patients (p = 0.04). (Author abstract) (29 Refs)

18. PRODUCTION OF ALPHA-FETOPROTEIN, NORMAL SERUM PROTEINS, AND HUMAN CHORIONIC GONADOTROPIN IN STOMACH CANCER: HISTOLOGIC AND IMMUNOHISTOCHEMICAL ANALYSES OF 35 CASES.

Kodama T, Kameya T, Hirota T, Shimosato Y, Ohkura H, Mukojima T, Kitaoka H
Pathology Div., Natl. Cancer Center Res. Inst., 5-1-1, Tsukiji, Chuo-ku, Tokyo 104, Japan
Cancer; 48(7):1647-1655 1981

By immunoperoxidase histochemical staining of formalin-fixed paraffin-embedded sections, the production of alpha-fetoprotein (AFP), albumin (ALB), transferrin (TF), alpha-1-antitrypsin (AAT), and human chorionic gonadotropin (HCG) was examined in 35 operatively resected stomach cancers with elevated serum AFP levels (higher than 20 ng/ml as determined by radioimmunoassay). Cells positive for AFP were found in 19 cases (54%). In 29 cases (83%), some tumor cells contained normal serum proteins (ALB, TF, or AAT). All 19 tumors with AFP-positive cells also stained positively for two or three kinds of normal serum proteins. In some cases, AFP and normal serum proteins were localized in the same cells. There were two cases in which metastatic tumors produced AFP, whereas the primary sites did not. In nine cases (26%), HCG was present in tumor cells and HCG- and AFP-positive cells were coexistent in six tumors. Histologic examination of AFP-producing stomach tumors revealed medullary or papillotubular arrangements with marked nuclear atypia and eosinophilic granular or clear cytoplasms containing no glycogen or mucin. Some tumors with medullary patterns resembled liver cell carcinomas. Concordant phenotypic expression of AFP and normal serum protein production appears to be a general feature of AFP-producing tumors such as liver cell carcinoma, yolk sac tumor, and stomach cancer. (Author abstract) (47 Refs)

REVIEWS/ OTHER RELATED STUDIES

19. TUMOR MARKERS.

Statland BE
No affiliation given
Diagn Med; 4(4):21-25,28,29,32,33,36,38 1981

Eleven groups of clinical chemistry analytes which have been used successfully in evaluating patients with cancer are reviewed. Oncofetal antigens used include alpha-fetoprotein, tissue polypeptide antigen, Tennessee antigen, fetal sulfoglycoprotein, pancreatic oncofetal antigen, and mammary tumor-associated glycoprotein. Pregnancy-associated proteins of diagnostic utility are human chorionic gonadotropin, pregnancy-specific glycoprotein, and pregnancy-associated alpha-Z-glycoprotein. Other proteins that are valuable as tumor markers include certain glycoproteins (eg those associated with sialic acid), acute phase reactants (eg haptoglobin, orosomucoid, and alpha-1-antitrypsin), ferritin, and casein. Enzymes synthesized by tumor cells include certain glycosyltransferases, placenta-like alkaline phosphatase, and prostatic acid phosphatase. Because bone and liver are frequent sites of metastatic carcinoma, enzymes derived from liver tissue and from bone tissue can be monitored. Osteolytic metastases (important in patients with breast cancer) are associated with the breakdown of collagen in bone; the relative urinary excretion of amino acid derivatives unique to collagen (vis hydroxyproline:creatinine ratio) is of diagnostic interest. Polyamines, nucleosides, cellular markers (eg T-cell and B-cell markers), and steroid receptors are also used for classification of malignancy. (42 Refs)

20. CLINICAL IMMUNOLOGY AND IMMUNOTHERAPY OF GYNECOLOGIC TUMORS (ONCOLOGY OVERVIEW).

International Cancer Research Data Bank
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Clinical Immunology and Immunotherapy of Gynecologic Tumors (Cancer Overview) Freedman, R S, ed This Title is Available Through National Technical Information Service, Springfield, VA, as NT ISUB/PB81-922802:; OT-81/02:52pp. 1981

Oncology Overviews are a service of the International Cancer Research Data Bank (ICRDB) Program of the National Cancer Institute. They are retrospective bibliographies containing 100-500 selected abstracts of published research on topics of high interest to cancer investigators. The scope of this Overview includes all clinical aspects of the immunology and immunotherapy of gynecologic tumors. Immunologic studies of gestational trophoblastic disease include paternal antigen expression, human leukocyte antigen histocompatibility, and immunoassays of betaglycoprotein and human chorionic gonadotropin (HCG). Antigenic studies of the uterine cervix include herpes viruses, cytomegaloviruses, tumor-associated antigens, carcinoembryonic antigens and beta oncofetal antigens. Studies of cellular immune response, lymph node morphology and lymphocytic infiltration as prognostic indicators of the uterine cervix are covered as well as the effects of radiotherapy on the immune status of patients with cervical carcinoma. Immunologic aspects of ovarian tumors which are covered include human ovarian tumor-associated antigens and oncofetal antigens. Non-specific, active specific, and other immunotherapeutic trials in gynecologic neoplasms are also included in this Overview.

21. CEA: BASIC CONCEPTS, CLINICAL APPLICATIONS.

Reynoso G
Dept. Pathology, Ideal/Wilson Medical Center, Johnson City, NY
Diagn Med; 4(4):41,42,46-48,51,54-57 1981

Review of diagnostic potential engendered in the association between oncogenesis and integrity of the immunocompetent system is supported by an assessment of carcinoembryonic antigen (CEA) and its clinical application. CEA is a glycoprotein that is abundant in entodermally-derived tissues (intestinal mucosa, pancreas, lung) and also found in non-entodermally derived tissues. Present in normal fetal tissues, it is also an oncofetal antigen, ie a tumor-associated antigen that reappears in adult cells and plasma during oncogenesis. CEA is the only immunological test for cancer with widespread clinical use. Biochemical characterization and tentative structure have been made. Many glycoproteins exhibit immunological cross-reactivity with CEA extracted from colonic carcinoma tissue; these glycoproteins are thought to belong to a single class of closely related antigens sharing four classes of antigenic determinants. Use of CEA in cancer screening programs for asymptomatic populations is not efficient: CEA appears in normal cells and incidence of antigenemia in healthy subjects increases with age and level of smoking. Neither the sensitivity nor specificity of CEA assays is high enough to justify its use alone as a diagnostic test; additional studies are needed in patients with consistently elevated levels of CEA. CEA can be used as an adjunct in cancer patient management, to aid in clinical staging and detect recurrence or relapse in surgically treated cases, and to monitor treatment in patients undergoing chemo- or radiotherapy. CEA is most reliable for monitoring colorectal cancer and possibly mammary and pancreatic carcinoma and neuroblastoma. (50 Refs)

22. CLINICAL APPLICABILITY OF DETERMINATION OF GESTATION-SPECIFIC PROTEINS IN BLOOD SERUM.

Kaminska JA, Ozuch B
Zaklad Medycyny Nuklearnej, Instytut Onkologii im. Marii Sklodowskiej-Curie, ul. Wawelska 15, 02-032 Warsaw, Poland
Ginekol Pol; 52(4):381-391 1981

Studies on gestation-specific proteins and their clinical applicability in the diagnosis and monitoring of pregnancy and neoplasma are reviewed. Elevated alpha-fetoprotein levels are encountered in the blood serum of patients with primary hepatic carcinoma, yolk-sac tumors, and endometrial sinus tumors. The carcinoembryonic antigen (CEA) levels are elevated in patients with cancer of the gastrointestinal tract, bronchi, urinary tract, breast, thyroid gland, and with malignant lymphoma and leukemia. Determination of the serum CEA level is especially suitable for the postoperative monitoring of patients with cancer of the large intestine. Determination of the human chorionic gonadotropin level is valuable in the diagnosis and monitoring of patients with choriocarcinoma. The pregnancy-specific protein SP-1 is a sensitive and early indicator of trophoblastic diseases (choriocarcinoma, hydatid mole, and chorioadenoma destruens) and of changes in the clincal course under the effect of therapy. (79 Refs) (In POL)

23. THE EFFECTS OF CONCOMITANT USE OF NEOCARZINOSTATIN (NCS) AND 5-FLUOROURACIL (5-FU) AS ADJUVANT CHEMOTHERAPY OF CANCER OF THE LARGE INTESTINE.

Yokomori T, Taniguchi T, Hisataka H, Kaneko H, Owada S, Saito K, Watanabe M
Dept. Surgery, Ojiya General Hosp., Ojiya-shi, Niigata Pref. 947, Japan
Gan To Kagaku Ryoho; 8(4):633-639 1981

Sixty postoperative patients with cancer of the large intestine (27 cases of colon cancer, 33 cases of rectum cancer) were given neocarzinostatin (NCS) in combination with 5-fluorouracil (5-FU) as adjuvant chemotherapy (NF-therapy) and studied for efficacy, side effects and changes of the serum carcinoembryonic antigen value during the therapy. Side effects occurred in 18 cases (30%). There was no difference in incidence of side effects among the various stages of cancer and the operative procedures. Side effects appeared to be more frequent between day 11 and 20 of initiation of treatment. General side effects were leukopenia (11.7%), thrombopenia (5.0%) anorexia

(6.7%) and diarrhea (6.7%). In 25 patients treated with nonradical surgery, 14 survived more than 12 mo and 2 more than 24 mo. Out of 23 evaluable cases on the basis of the assessment criteria of Karnofsky, 6 cases (26.1%) were placed in a group of O-A, O-B and O- C, and 8 cases (34.8%) were placed in a group of I-A and I-B. As for the correlation between the period of treatment and the survival duration, both Karnofsky effective cases and long surviving cases treated with surgical resection were mainly observed in the long NF-therapy group. Both the cured patients treated with surgical resection and the patients who showed a high value of serum CEA before surgical resection were placed in Stage I-IV and these showed normal values of serum CEA during the NF-therapy. On the other hand, the noncured patients treated with surgical resection were placed in Stage IV-V and showed variability in serum CEA particularly; the cases with liver metastasis did not show a tendency to decrease in CEA value after NF-therapy. (15 Refs) (In JPN)

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ONCOFETAL PROTEINS

SERIES CB01 No. 82/03

MARCH, 1982

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STRUCTURE/ IDENTIFICATION/ CHARACTERIZATION

1. A COMPARISON OF THE PHYSICOCHEMICAL PROPERTIES OF CARCINOEMBRYONIC ANTIGEN IN EXTRACTS OF TUMOUR TISSUE, ASCITIC AND CYST FLUID FROM OVARIAN CANCER.

Hill R, Daunter B, Magon H, Khoo SK, Mackay EV

(c/o Khoo) Dept. Obstetrics and Gynecology, Univ. Queensland, Royal Brisbane Hosp., Clinical Sciences Building, Herston, Queensland 4029, Australia

Aust J Exp Biol Med Sci; 59(4):469-476 1981

In view of the reported disagreement in the physicochemical properties of ovarian carcinoembryonic antigen (CEA), this study was undertaken to compare the properties of CEA obtained from extracts of ovarian tumor tissue, ascitic fluid and

cyst fluid. On the basis of mol wt estimation and binding properties with Concanavalin A and wheat germ lectin, ovarian CEA from these three source appear ed similar, and also possessed similar properties to those of colonic CEA. On isoelectric focusing, however, it was found that the isoelectric point of CEA from tumor tissue and cyst fluid differed from that from ascitic fluid. It is most likely that this is due to a loss of sialic acid from the CEA released into ascitic fluid. (Author abstract) (28 Refs)

ASSAY PROCEDURES/ SYNTHESIS

2. ENDODERMAL SINUS TUMOUR AND ALPHAFOETOPROTEIN PRODUCTION BY OVARIAN TUMOURS (MEETING ABSTRACT).

Talerman A
Department of Pathology, University of Chicago, Chicago, IL
Eighth European Congress of Pathology, August 30-September 4, 1981, Helsinki, Finland. The Congress 92 pp., 1981.

Endodermal sinus (Yolk sac) tumor (EST) became established as a distinctive type of germ cell neoplasm due to the exhaustive studies of Gunnar Teilum. He showed that homologous tumors showing the histological appearances of EST are found in the ovary, testis, and the extragonadal sites where germ cell tumors are known to occur. Although EST occurs in pure form, it is frequently associated with other neoplastic germ cell elements forming a mixed germ cell tumour. It has been shown that in the ovary EST is the second most common malignant germ cell neoplasm occurring from birth to the menopause. The recent finding that EST is associated with Alphafetoprotein (AFP) synthesis, which also occurs in the normal yolk sac during embryogenesis gave further support to the view that EST is a well differentiated but highly malignant germ cell neoplasm differentiating from embryonal carcinoma along the vitelline pathway. AFP has been shown to be a very good and specific tumor marker for EST, and it can be used for confirming the diagnosis, early detection of metastases and recurrences, and for monitoring the efficacy of therapy. (no Refs)

3. COMPARATIVE STUDIES OF CARCINOEMBRYONIC ANTIGEN (CEA) METHODOLOGY USING ENZYME IMMUNOASSAY (EIA) AND RADIOIMMUNOASSAY (RIA) PROCEDURES (MEETING ABSTRACT).

Gabriel NS, Hicks JT, Madera-Orsini F
Department of Pathology, Oak Park Hospital, Oak Park, IL, 60302
Clin Chem; 27(6):1079 1981

Due to the time-consuming and elaborate procedures of the commercially available CEA-Roche RIA, a study was undertaken to evaluate and compare other recently available (Abbott) CEA procedures. We evaluated the two methods offered by Abbott Laboratories involving RIA and EIA versus the established CEA-Roche RIA method. Results obtained with ROCHE and ABBOTT procedures generally agree and have a correlation coefficient of 0.90 +/-0.05 in all ranges. Precision studies indicate that the ABBOTT EIA procedure has comparable or improved precision with fewer unacceptable assays than ROCHE RIA. Recovery studies were performed in duplicate on 30 samples using the three techniques. Recoveries obtained were in the range of 90- 102% with the three methods. The inter-assay reproducibility of the three methods using three different controls (Roche) in paired determinations was not significantly different, with the ABBOTT EIA, having the lowest % CV. The intra-assay reproducibility using the same controls again showed ABBOTT-EIA with the lowest % CV. We conclude that ABBOTT EIA procedure is the method of choice for the determination of CEA in the clinical laboratory. It eliminates the use of dialysis, columns or radionuclides and the reagents have longer shelf-life. It requires none or minimal reagent preparation, eliminating problems with pH sensitivity and ionic strength. Serum or plasma can be used without interference from heparin, citrate, EDTA or lipemia. Concentrations of CEA up to 60 ng/ml can be quantitated directly without the use of dilutions. (no Refs)

4. EVALUATION OF AN ENZYME IMMUNOASSAY (EIA) TECHNIQUE FOR THE MEASUREMENT OF CARCINOEMBRYONIC ANTIGEN (CEA) IN SERUM (MEETING ABSTRACT).

Mitra R, Oxenhandler RW, Parker KM, Pape BE, Truelove C
Department of Pathology, University of Missouri Health Sciences Center, Columbia, MO, 65212
Clin Chem; 27(6):1079 1981

Carcinoembryonic antigen (CEA) is a well recognized marker of the progression of malignant disease and the effectiveness of therapy. Clinical measurement of CEA in the US was limited to conventional radioimmunoassay (RIA) until the recent introduction of solid-phase RIA and solid-phase EIA systems. We evaluated the analytical and clinical performance of the Abbott CEA-EIA. Within-assay precision assessed from 20 replicates was 8.0% and 5.4% for serum concentrations of 3.3 and 8.0 ng/mL, respectively. Between-assay precision estimated from 12 replicates of the 3, 10, and 20 ng/mL standards and two serum pools containing 5.2 and 11.5 ng/mL, was 6.8%, 5.1%, 6.7%, 10.2% and 5.7% respectively. Recovery of CEA added to nine serum specimens av 98.8%. Since high levels of CEA are frequently present and the highest standard is 20 nanograms, it is important that comparable results be obtained when specimens are diluted. Nine specimens were analyzed at multiple dilutions and the final results, when corrected for dilution, were in excellent agreement. To compare EIA with the Abbott RIA method, 41 serum specimens were analyzed by both methods. Regression analysis of data gave the equation EIA equals 1.0 RIA + 13.0 (r equals 0.99). Clinical impressions were in good agreement with the patient CEA-EIA results. We conclude that the performance characteristics of the CEA-EIA method indicates that it is an acceptable alternative to the RIA methods for measuring CEA in serum. (no Refs)

5. A COMPARISON OF THREE CEA IMMUNOASSAY METHODS (MEETING ABSTRACT).

Tercero JC, Nelson JC, Chi E, Broughton A
Nichols Institute, San Juan Capistrano, CA, 92675
Clin Chem; 27(6):1079 1981

Two sandwich immunoassays using the same antibody and standard, one enzyme-labeled (EIA) and the other 125I-labeled (RIA-A) (Abbott Laboratories) and a Zirconyl gel radioimmunoassay with a 125I label but using a different antiserum and standard (RIA-R) (Roche Diagnostics) were studied. Consecutive unknown plasma were analyzed in a single line study for method to method comparisons. One hundred seventy-nine were assayed by both EIA and RIA-A; 228 were run by both RIA-A and RIA-R; 395 were run by both RIA-R and EIA. The correlation between the two sandwich techniques was greater than the correlation between the two radioimmunoassays or between the enzyme immunoassay and the radioimmunoassay employing a different antisera and standard. The correlations among the other assays were comparable but the categorical discordance of the RIA-R for the EIA was 22% compared to that of the RIA-R with the RIA-A which was only 8%. These data support the concept that the change in label alone provides comparable assay results but a change in antigen and antibody provides significant discordance. (no Refs)

6. ANALYTICAL EVALUATION OF ABBOTT AND ROCHE CEA ASSAYS (MEETING ABSTRACT).

Stein KE, Valdes R
Division of Biochemistry, Department of Pathological Laboratory Medicine, Jewish Hospital, St. Louis, MO, 63110
Clin Chem; 27(6):1079 1981

We present data evaluating and comparing two carcinoembryonic antigen (CEA) radioimmunoassay methodologies; CEA-Roche and Abbott-CEA. Assay performance is characterized for reproducibility, recovery, CEA extraction efficiency, dilution parallelism, and method sensitivities. Roche CEA assays are performed utilizing the Amicon MC-40 diafiltration system. Analytical intra-run precision, determined for control material (Bio-Rad) and pooled human plasma, for the Roche Assay is 18% and 14.3% for concentrations of 1.8 and 9.6 ng/mL respectively. CEA added prior and subsequent to the recommended extraction procedures gives av recoveries of 85% and 94% respectively for the Abbott method. Plasma dilution over a wide range of concentration, 0.6 to 765 ng/mL, yields a linear correlation, observed (y) vs expected (x), y equals 0.96x + 0.3 ng/mL for Abbott and Y equals 1.04x + 5.4 ng/mL for Roche utilizing the indirect method and diluting dialysates for greater than 20 ng/mL. Corresponding regression analysis for values greater than 20 ng/mL utilizing the Roche direct assay was y equals 1.30x + 9.2 ng/mL indicating values at least 30% higher than expected by contrast to the indirect procedure or the Abbott method. The Abbott and Roche assay sensitivity coefficients for concentrations less than 5 ng/mL are 200 and 3,200 CPM per ng/mL respectively. In summary, comparable precision and dilution linearity are achieved by both assays as we perform them, provided the Roche assay utilizes the indirect method with dialysate dilution for values greater than 20 ng/mL, otherwise significant differences are observed. (no Refs)

7. A COMPARISON AND PRECISION STUDY OF TWO COMMERCIAL COMPANIES FOR THE QUANTITATIVE MEASUREMENT OF CARCINOEMBRYONIC ANTIGEN (CEA) (MEETING ABSTRACT).

Berk L S, Imperio N, Eby B
Loma Linda University Medical Center, Loma Linda, CA, 92350
Clin Chem; 27(6):1079 1981

We evaluated Abbott Labs CEA and compared it with Roche Diag's column CEA. Abbott's CEAs are solid phase immunoassays based on the sandwich principle and employ either an enzyme immunoassay (EIA) or radioisotope as the label. Roche's CEA is a standard radioimmunoassay (RIA). All samples were assayed by the protocols provided by the manufacturers. For interassay precision studies, a series of select samples were run in five separate assays. For a comparison study different patient sera were assayed with Abbott EIA and Roche RIA n equals 40, r equals 0.9123, slope 1.1037 and intercept-0.7063. The comparison study had approx 10% of the specimens significantly (not all clinically) different in concentrations. In conclusion, the reasons for the differences in methods are uncertain but are generally reproducible and may represent different extraction methods, different antigen sources and antibody specificity. The EIA does not require dialysis or radioisotopes, an advantage to chemistry labs not possessing a radionuclide license. In our lab the Abbott procedure has provided improved precision with fewer unacceptable results. The major clinical role for CEA measurement is in preoperative tumor staging and in monitoring for recurrence of cancer. Therefore, it is suggested that a lab follow patients with serial CEA assessment with one manufacturer and not interchange. (no Refs)

EXPERIMENTS IN ANIMAL SYSTEMS

8. HETEROGENICITY AND SPECIFICITY OF TUMOR ASSOCIATED ANTIGENS (TAA) AND FETAL ANTIGENS (FA) AS DETECTED BY 51CR-LAI TEST AND EM TEST IN MOUSE SARCOMA.

Werner H, Schulze HA
Res. Unit Immunology, Wilhelm Pieck Univ., DDR-2500 Rostock, E. Germany
Arch Geschwulstforsch; 51(6):481-484 1981

Murine tumor associated antigens (TAA) and fetal antigens (FA) were characterized by immunological methods. Antigens were obtained from fetuses at the 10th-14th day of gestation and chemically-induced sarcomas from CBA, B10D2 mice. Soluble extracts were prepared and separated using the Ultrogel AcA 34. Single antigen fractions were incubated with spleen cells from pregnant or tumor-bearing mice. Response was measured by 51Cr lymphocyte adherence inhibition (LAI)and electrophoretic mobility (EMT) tests. Different antigen activities were found for three antigen fractions: P1 (mol wt 200,000-250,000), P2 (mol wt 120,000-160,000), and P3 (mol wt 50,000-60,000). EMT correlated with LAI for P2, but not for P1 or P3. LAI det ected some specific components of P1, but failed to detect a common tumor type specificity in P3. Pregnancy specificity was localized in the P2 fraction of FA. (6 Refs)

9. T-CELL-MEDIATED ANTITUMOR IMMUNE RESPONSE INDUCED BY ONCOFETAL ANTIGENS.

Gautam S, Deodhar SD
Dept. Immunopathology, Cleveland Clinic Foundation, 9500 Euclid Ave., Cleveland, OH, 44106
JNCI; 67(4):939-945 1981

The possibility that fetal antigens take part in tumor immunity has been investigated to a limited extent, but the results of these studies have been controversial. It is not clear that tumor inhibition shown in some systems is due to an immune reaction. In the present study, performed in a weakly immunogenic tumor system (Lewis T241 fibrosarcoma in inbred C57BL/6J mice), immunization of mice with syngeneic fetal cells resulted in striking inhibition of growth and metastases of tumors. Mice that had gone through single pregnancies also showed a decreased rate of tumor growth and tumor metastases. Further studies have shown that the tumor inhibitory response evoked by fetal cell immunization is due to fetal antigens, and the male specific HY antigen is not responsible for antitumor response. Injection of tumor cells mixed with spleen cells from mice immunized with syngeneic fetal cells into normal mice resulted in significant inhibition of tumor growth and metastases in the Winn neutralization assay. Syngeneic fetal cells, normal adult spleen cells, or spleen cells from C57BL/6 mice immunized with allogeneic fetal cells did not inhibit tumor growth or metastases. These results show that tumor inhibition following fetal cell immunization is due to an immune reaction and is not due to a nonimmune physiologic process. Further analysis of effector cells showed them to be of the T-cell type. (Author abstract) (23 Refs)

10. REGULATION OF ALPHA-FETOPROTEIN AND ALBUMIN BIOSYNTHESIS IN MURINE HEPATOMA CELLS BY DIMETHYLSULFOXIDE (MEETING ABSTRACT).

Higgins PJ
Laboratory of Cell Biochemistry, Memorial Sloan-Kettering Cancer Center, New York, NY
Thirteenth Miami Winter Symposium: Cellular Responses to Molecular Modulators, January 12-16, 1981, Miami, Florida. University of Miami 112 pp., 1981.

The effect of the polar solvent dimethylsulfoxide (DMSO) on the synthesis and secretion of liver-specific (albumin) and tumor-associated (alpha-fetoprotein; AFP) gene products was studied in an established line of mouse hepatoma cells (BW1). DMSO produced a concentration-dependent decrease in final hepatocyte population density which was accompanied by a significant increase in total extractable protein per cell. Approx 0.51 and 0.53% of the total BW1 cellular protein consisted of AFP and albumin, respectively. Incubation of BW1 cells with DMSO led to a marked enhancement in both the albumin and AFP contribution to total cell-associated protein (42 and 94% for albumin and 118 and 154% for AFP in 0.5 and 1% DMSO-containing growth medium, respectively) and in the extra-cellular accumulation of these proteins. The level of albumin production by BW1 cells increased with exposure to increasing concentrations of DMSO in the growth medium. AFP synthesis, in contrast, was maximal in 0.5% DMSO-containing medium and was not further stimulated (and actually decreased) upon exposure of the cells to higher concentrations of the polar solvent. Although AFP and albumin are two hepatocyte gene products which are biochemically and, possibly, functionally similar, the biosynthetic regulation of these two proteins in DMSO-stimulated hepatocytes is quite different. Polar solvent-stimulated hepatocyte cell cultures may, thus, serve as an appropriate model system to study basic mechanisms in the regulation of tissue-specific and tumor-associated gene expressions in vitro. (no Refs)

IMMUNOLOGIC INTERACTIONS

11. ESTABLISHMENT OF LEUKOCYTE SENSITIZATION TO CARCINOEMBRYONIC ANTIGEN IN RECTAL CANCER.

Novikov DK, Shmakov AP
Medical Inst., Vitebsk, USSR
Vopr Onkol; 27(8):40-45 1981

Aqueous-saline extracts of autologous rectal tumor tissue inhibited WBC migration in 7 out of 10 patients with rectal tumors in autoplasm-containing medium, and in 5 out of 11 patients - in control serum. Antigens of allogenic rectal tumors inhibited WBC migration (LMI) in 4 out of 5 patients (Stage II), in 15 out of 21 patients (Stage III), and in 5 out of 10 patients (Stage IV) in control serum medium, and in none of control patients. WBC sensitization to mucosal antigen was established only in 8% of patients (Stage II-IV), in control serum medium. LMI in medium containing autoplasm and control serum was observed in 24 out of 36 patients. Extracts obtained from human embryonal liver inhibited WBC migration in 14 out of 27 patients (Stage II-IV), including 3 cases in which WBC did not respond to tumor-associated antigen. LMI by carcinoembryonic antigen was registered in a total of 31 out of 36 cases (86%). In five cases out of seven, unresponsive WBC of patients with rectal tumors did respond to tumor-associated antigen by inhibiting WBC migration, after re-incubation at low temperature, in a medium free from autologous blood plasma. (Author abstract) (18 Refs) (In RUS)

CLINICAL/ DIAGNOSIS/ IMMUNOTHERAPY

12. PLASMA LIPID-BOUND SIALIC ACID AND CARCINOEMBRYONIC ANTIGEN IN CANCER PATIENTS.

Dnistrian AM, Schwartz MK
Dept. Biochemistry, Memorial Sloan-Kettering Cancer Center, New York, NY, 10021
Clin Chem; 27(10):1737-1739 1981

We evaluated lipid-bound sialic acid as a 'marker' in cancer patients and assessed the individual and combined value of lipid-bound sialic acid and carcinoembryonic antigen determinations in these patients. Plasma was sampled from 62 normal subjects and 125 cancer patients. Lipid-bound sialic acid was determined by the resorcinol method after total lipid extraction and isolation of the sialolipid fraction from plasma. Neither marker was increased in many breast cancer patients. Carcinoembryonic antigen was increased more commonly and to a greater degree in colon cancer patients and seems to be the preferred marker. Both markers were increased in lung cancer patients and their combined evaluation improved the rate of detection. Lipid-bound sialic acid was increased in more patients with leukemias, lymphomas, Hodgkin's disease, and melanomas, suggesting that it may be a useful biochemical marker in these types of cancer. (Author abstract) (8 Refs)

13. AFP SERO-SURVEY AND EARLY DIAGNOSIS OF LIVER CELL CANCER IN THE QIDONG FIELD..

Zhu Y
Jiangsu Qidong Inst. Liver Cancer, Qidong, People's Republic of China
Zhonghua Zhongliu Zazhi; 3(1):35-38 1981

Results of a mass survey and early diagnosis of liver cancer using serum alpha fetoprotein (AFP) are described. Of 1,786,906 persons tested between 1971 and 1977, liver cancer was discovered in 1,026. With sensitive assay technics for AFP, the positive rates for liver cancer reaches 96.3%. An incidence rate of Stage I liver cancer in single surveys was found to be about 35% that increased to 76% in regular twice-a-yr surveys. The postoperative 2-yr survival rate of Stage I liver cancer patients was 69%. The 5-yr survival rate of 117 surgical cases of liver cancer was 26%. (7 Refs) (In CHI)

14. CEA, HCG-BETA AND ALPHA-FETOPROTEIN: CLINICAL SIGNIFICANCE OF TUMOR MARKERS.

Nagel R, Borgmann V, Kemper JD
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Helv Chir Acta; 48(3/4):433-443 1981

The clinical significance of the tumor markers carcinoembryonal antigen (CEA), human choriogonadotropin-beta (HCG-b), and alpha1-fetoprotein (AFP) were studied based on 85 clinical cases and literature. CEA was associated with tumors of the colon, stomach, bronchi, breast, prostate, and bladder, as well as hypernephroid tumors, and was too nonspecific for diagnosis of testicular tumors. Of 19 patients with teratocarcinoma, 57.9% were AFP-positive and 52.6% were HCG-b-positive. Of 38 patients with embryonal carcinoma, 73.7% were AFP-positive and 63.2% were HCG-b-positive. Of 23 patients with seminoma, only 1 (4.4%) was HCG-b-positive. No seminoma patients were AFP-positive. Simultaneous determination of HCG-b and AFP resulted in 85% positive for nonseminoma testicle tumors. Although AFP and HCG-b are not specific enough for marker-oriented therapy, they are important for diagnosis, therapy planning, and case control, and as indicators of metastasis. (29 Refs) (In GER)

15. VALUE OF CARCINOEMBRYONIC ANTIGEN DETERMINATION IN MAMMARY CANCER.

Carrion P, Avila C, Massieu C, Curto M
Seccion Oncologia Medica, Centro Especial 'Ramon y Cajal', Madrid, Spain
Oncologia; 6(4):14,17-18,20-21 1981

Carcinoembryonic antigen (CEA) determination for early diagnosis of relapse after mastectomy and for monitoring effects of hormone and/or chemotherapies is evaluated. Of 140 mammary cancer patients, 9 with localized cancer were tested before and after surgery (Group I), 79 with localized cancer were tested 1, 3, 6, 12, and 24 mo after surgery (Group II), and 52 with advanced cancer (5 having distant metastases) were tested 10-21 days after the end of therapy (Group III). All patients received Halsted or Patey radical mastectomy; axillary adenopathies were examined histologically. Lymph node-positive patients received polychemotherapy and antiestrogen therapy for 6 mo. Patients with metastases were treated with different hormone therapy and chemotherapy. In Group I five patients exhibited elevated CEA which became normal after surgery, but later three of them developed metastases. In Group II 67 patients remain clinically free of disease, although 10 had elevated CEA values (greater than 50 mg in 2 cases). The remaining 12 patients developed metastases although CEA was normal in 8 and elevated in 4; 11 of the patients had axillary metastases with greater than 4 positive lymph nodes. In Group III 33 patients had elevated CEA (greater than 25 mg in 25 cases). CEA was elevated in 100% of hepatic, 83.3% of lung, and 72.2% of bone metastasis cases. Hormone therapy and/or chemotherapy was monitored in 25 patients; 80% of remissions and relapses could be followed by CEA. (12 Refs) (In SPA)

16. SEQUENTIAL GALACTOSYLTRANSFERASE AND CARCINOEMBRYONIC ANTIGEN LEVELS IN ADVANCED BREAST CARCINOMA.

Paone JF, Baker RR, Waalkes TP, Shaper JH
Dept. Surgery, Johns Hopkins Hosp., Baltimore, MD, 21205
J Surg Res; 31(4):269-273 1981

UDP-galactosyltransferase (GT), an enzyme that functions in the biosynthesis of glycoproteins, has recently been found to be a sensitive biologic tumor marker. In the present study, sequential GT levels were compared to simultaneous CEA determinations to establish which biomarker more accurately reflects changes in tumor activity in patients receiving therapy for advanced breast carcinoma. Serum levels of GT and CEA were measured each mo in 38 patients undergoing combination chemotherapy for metastatic breast carcinoma. The results were correlated with the objective responses observed to chemotherapy during this period. Prior to the institution of chemotherapy, significant serum GT elevations were observed in 84.2% (32/38) of the patients, while 55.3% (21/38) had elevations in levels of CEA. During therapy 71.4% (10/14) and 50% (7/14) of the GT and CEA levels, respectively, decreased in patients who had an objective response to therapy. In the patients whose disease progressed on therapy, 75% (18/24) had significant increases in GT levels during this interval, while 41.6% (10/24) had increases in CEA (p less than 0.01). Furthermore, in 11 patients (29.5%) serum GT alterations correctly reflected changes in tumor activity, while CEA levels remain static. These data indicate that GT is more sensitive than CEA as a marker for breast carcinoma and suggest that GT may be clinically useful in the management of patients with metastatic breast disease. (Author abstract) (21 Refs)

17. THE VALUE OF TUMOR MARKERS IN CANCER OF THE OVARY.

Cantarow WD, Stolbach LL, Bhattacharya M, Chatterjee SK, Barlow JJ
(c/o Stolbach) Pondville Hosp., P.O. Box 111, Walpole, MA, 02081
Int J Radiat Oncol Biol Phys; 7(8):1095-1098 1981

Tumor markers identified in the patients with ovarian cancer are reviewed. Current list of markers includes ovarian cystadenocarcinoma-associated antigen, galactosyltransferase, cystine aminopeptidase, carcinoplacental alkaline phosphatase, carcinoembryonic antigen, alpha-fetoprotein, and human chorionic gonadotropin. Although these markers fail to meet the criteria for early detection of ovarian cancer, they can be used in the immunodetection, monitoring of the therapy, and possibly in the immunotherapy. (35 Refs)

18. THE SUPPRESSION OF PHOSPHATASES AND CARCINOEMBRYONIC ANTIGENS IN SERUM AFTER SPECIFIC IMMUNOTHERAPY FOR METASTASIZING CARCINOMA OF THE PROSTATE.

Rothauge CF, Kraushaar J, Gutschank S, Weidner W, Krause W
Zentrum fur Chirurgie, Anasthesie und Urologie, Feulgenstrasse 2, D-6300 Giessen, W. Germany
Helv Chir Acta; 48(3/4):453-458 1981

The effect of specific immunotherapy for metastatic carcinoma of the prostate was measured using determination of serum prostatic acid phosphatase (PAP) and carcinoembryonic antigen (CEA) by conventional enzymatic (EA) and radioimmunoassay (RIA) methods. Measurements were made before and after therapy. One wk after vaccination CEA and PAP as measured by EA and RIA methods showed a sharp decline from pretreatment values. CEA and PAP levels rose after 1 wk, but dropped again sharply after revaccination. Declines in CEA and PAP corresponded to improved clinical findings, which included histologically and cytologically determined tumor regression and scintigraphically determined shrinkage of rib metastases. PAP determination was more useful for immediate control of therapy, while CEA was more useful for follow-up studies. Although RIA determination of PAP was not satisfactory in the early stages of prostate cancer, it was more suitable for follow-up studies than conventional EA. (13 Refs) (In GER)

19. EXPERIMENTAL RADIOIMMUNOTHERAPY OF A XENOGRAFTED HUMAN COLONIC TUMOR (GW-39) PRO DUCING CARCINOEMBRYONIC ANTIGEN.

Goldenberg DM, Gaffar SA, Bennett SJ, Beach JL
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Cancer Res; 41(11,part1):4354-4360 1981

Experiments were undertaken to evaluate the antitumor effects of 135I-labeled goat antibody Ig G prepared against carcinoembryonic antigen in hamsters bearing the carcinoembryonic antigen-producing GW-39 human colonic carcinoma. At a single injection of 1 mCi 131I and higher, a marked growth inhibition of GW-39 tumors, as well as a considerable increase in the survival time of the tumor-bearing hamsters, could be achieved. At a dose of 1 mCi, the radioactive affinity-purified antibody appeared to be superior to radioactive normal goat Ig G in influencing tumor growth and survival time, but no significant difference could be seen at the higher dose of 2 mCi given. Radiobiological calculations indicated that the tumors received, at up to 20 days after therapy, 1,325 rads for the specific antibody and only 411 rads for the normal Ig G preparation. These findings encourage the further evaluation of antibodies to tumor markers for isotopic cancer therapy. (Author abstract) (36 Refs)

20. LOCALISATION OF HUMAN TUMOURS BY EXTERNAL SCANNING AFTER INJECTION WITH RADIOLABELLED ANTIBODY TO AFP (MEETING ABSTRACT).

Fairweather DS, Halsall AK, Hine KR, Howell A, Dykes PW, Bradwell AR, Blackburn J, Reader A
Departments of Medicine, Oncology, Immunology and Medical, Physics Queen Elizabeth Medical Center and the General Hospital, Birmingham, England
Br J Cancer; 43(5):726 1981

Alpha-fetoprotein (AFP) is used as a tumor marker in germ-cell tumors. This preliminary study was carried out to assess whether deposits of these tumors could be identified by external scanning after injection of radio-labelled antibody to AFP. A total of 15 scans were performed on 12 patients, 10 with malignant teratoma, one with an endodermal sinus tumor and one with a seminoma (used a negative control). All 9 patients with high serum AFP gave positive scans; 5 of these at the time of diagnosis. All abnormal areas were confirmed by computerized tomography (CT) scans and lymphangiography, although 4 secondary deposits were missed. Three patients gave normal scans when studied again after successful treatment, and when the serum AFP had fallen to normal. A further 5 studied for the first time after treatment (4 with high serum AFP) gave positive scans, 3 of which were confirmed by CT scanning. Two areas of anti-AFP uptake over the stomach were not confirmed by the CT scans. These preliminary results show that it is possible to identify tumor deposits using antibody to AFP. (no Refs)

21. SERUM FERRITIN AS A THIRD MARKER IN GERM-CELL TUMOURS (MEETING ABSTRACT).

Grail A, Bates G, Milford-Ward A, Hancock BW
Royal Hallamshire Hospital, Sheffield, England
Br J Cancer; 43(5):726 1981

Serial measurements of serum ferritin have been assessed as an additional diagnostic and prognostic marker in a study of 12 patients with germ-cell tumor. The standard markers, serum alpha-fetoprotein (AFP) and beta human chorionic gonadotropin (hCG) levels. Falls and maintenance of normal levels of serum ferritin indicated favorable response to treatment; rising values were associated with recurrence of dissemination of tumor. The metabolic rates of decay of AFP and beta hCG give valuable indications of residual tumor, when values exceed the normal half-life values of less than 5 days for AFP and less than 24 hr for beta hCG. Although AFP and beta hCG are useful as markers in the follow-up of patients, increasing levels suggesting recurrent tumor, falls to within the normal range do not necessarily indicate a disease-free state. Chemotherapy may convert the tumor to a non-marker-producing form and/or may selectively eradicate the clone of marker-producing cells. Due to heterogeneity in metastases, production of tumor markers from different sites may vary. Possible explanations for the high serum ferritin level in malignancy include reticuloendothelial block of iron release, tissue damage and increased synthesis by the tumor. Even if serum ferritin cannot be classed specifically as tumor product, it is useful in the early detection of recurrent tumor and extragonadal progression of disease. (no Refs)

22. PRACTICAL APPLICATIONS OF MONOCLONAL ANTIBODIES AGAINST CARCINOEMBRYONIC ANTIGEN (CEA) (MEETING ABSTRACT).

Mach JP, Buchegger F, Phan M, Forni M, Ritschard F, Accolla R, Carrel S

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Ve Colloque International de Radioimmunologie de Lyon, April 9-11, 1981, Lyon, France. Centre de Medecine Nucleaire 101 pp., 1981.

Monoclonal antibodies against CEA produced by hybrid cells derived from fusion between spleen cells from mice immunized with purified CEA and cells from the P3-NSI/1-Ag4 myeloma were purified from hybridoma ascites by ammonium sulfate precipitation and DE-52 chromatography. The purified antibodies which had been shown to have a high specificity and affinity for CEA were tested for two major practical applications. First, they were used to develop a solid-phase enzymeimmunoassay capable of detecting 0.6-1.2 ng per ml of patient serum which proved as efficient as the presently available radio- and enzymeimmunoassay. Second, they were labelled with 131I and injected into tumor bearing patients in order to study the tumor localization of the antibodies. The results from these pilot studies, obtained by external scanning of the patients and by direct measurement of the radioactivity in resected tumors and adjacent normal tissues, showed that monoclonal anti-CEA antibodies are capable of specific tumor localization in some patients. Ten out of 20 patients with colon carcinoma injected with labeled monoclonal antibodies showed positive 'immuno-scintigraphy'. The specificity indices of localization obtained by comparing in fragments of tumor and normal tissues, the 131I radioactivity of the antibodies with the 125I radioactivity of control normal mouse IgG injected simultaneously with the antibodies, gave values ranging from 2-5. These encouraging results, however, are not sufficient to recommend this method of immuno-scintigraphy for routine tumor detection. (no Refs)

23. ONCOFETAL PROTEINS AS PROGNOSTIC INDICATORS IN BREAST CARCINOMA (MEETING ABSTRACT).

Halter S
Vanderbilt University, Nashville, TN

Monoclonal Antibodies and Breast Cancer, July 29, 1981, Bethesda, Maryland Breast Cancer Task Force Committee; 1981

In addition to certain biological properties such as invasion and angiogenesis, fetal and malignant cells may also share similar antigenic determinants. Because these antigens may confer on the fetus the ability to resist maternal rejection, the possession of similar or identical antigens may also protect malignant cells. We have been examining mammary carcinomas for the presence of several oncofetal and tumor associated antigens. One hundred fifteen cases of stage II mammary carcinoma have been assessed for carcinoembryonic antigen (CEA) and beta-one-glycoprotein (pregnancy specific) using an immunoperoxidase technique. Patients were divided into short survivors (survival less than three yr) and long survivors (greater than ten yr). Ninety percent of the tumors were infiltrating ductal carcinomas. The av age of the patients was 53 having an av of four positive axillary lymph nodes. Sixty-eight percent of the cases were positive for CEA. All positive cases showed focal distribution of CEA with scattered negative malignant cells. Statistical analysis showed no significance for the CEA positivity and short survival. Thirty-one percent of the cases were positive for beta-one pregnancy specific glycoprotein. Positive cases had cytoplasmic distribution of the marker. Statistical analysis showed no significant correlation between pregnancy specific glycoprotein positivity and patient survival. These antisera represent only two of a number of possible antigens shared by fetal and malignant tissues. (no Refs)

24. VALUE OF THE TISSUE POLYPEPTIDE ANTIGEN (TPA) DETERMINATION IN MAMMARY CARCINOMA (MEETING ABSTRACT).

Doepp M, Laubenberger Th
No affiliation given

Eur J Nucl Med; 6:49 1981

The determination of carcinoembryonic antigen is well established in the staging of mammary carcinoma (MC). The new oncofetal antigen TPA is considered to have a higher positive incidence than carcinoembryonic antigen. We investigated 87 women with MC who were diagnosed by histology, lung x-ray, liver scan, whole body bone scan, and liver ultrasound. Five groups were formed: 1) pre-op without metastases (M), 2) pre-op with M, 3) post-op without M, 4) post-op with M, 5) post-op with uncertain M. Results: TPA concentrations of the 5 groups: 1) 127 +/-32, 2) 231 +/-112, 3) 56 +/-19, 4) 214 +/- 97, 5) 83 +/-23. Upper limit of normals (3) is 90, as found in previous studies. The correlation between the number of M and the TPA is positive: R equals + .56, high significance. Two cases of (4) had to be excluded because of excessive TPA of 1000 U/L. They had additionally colon cancer some yr before, presumably with M from that origin. Group (5) could be subdivided in 3 cases with strong and 4 cases with light suspicion by means of TPA. Without group (5), the sensitivity of the TPA resulted in 65%, the specificity in 93%, and the predictive accuracy in 100%. Thus, an elevated TPA proves malignant growth, a normal value does not exclude it. (no Refs)

25. BIOLOGICAL DIAGNOSIS OF THE HEPATOCELLULAR CARCINOMA ASSOCIATED WITH LIVER CIRRHOSIS: CLINICAL AND EXPERIMENTAL STUDY (MEETING ABSTRACT).

Munoz M, Amiguet JA, Conchillo F, Prieto J, Liso P
Department of Medicine, University Clinic, University of Navarra, Pamplona, Spain

Gut; 22(5):A443 1981

Hepatocellular carcinoma develops frequently from liver cirrhosis and it is often very difficult to diagnose clinically. With this in mind we studied two oncofetal antigens (carcinoembryonic antigen and alpha-fetoprotein) and five acute-phase reactants (alpha-1-acid glycoprotein, alpha-1-antitrypsin, haptoglobin, ceruloplasmin and alpha-2-macroglobulin) in 10 patients with hepatocellular carcinoma associated with liver cirrhosis. As controls we used 56 healthy subjects and 58 patients who had liver cirrhosis without hepatocellular carcinoma. We found that the hepatocellular carcinoma associated with liver cirrhosis can be biologically differentiated from liver cirrhosis by the positivity of the alpha-fetoprotein and by a significant increase of haptoglobin and the other four acute phase reactants. Moreover, regular determinations of haptoglobin in patients with liver cirrhosis showed us that, in four cases, a rise in the haptoglobin level correlated with malignity. Furthermore, an experimental study of haptoglobin in rats with liver cirrhosis and with liver cirrhosis plus hepatocellular carcinoma confirmed these results. In conclusion, acute-phase reactants and alpha-fetoprotein are good biological indicators for the diagnosis of hepatocellular carcinoma which has developed from liver cirrhosis. (no Refs)

26. COMPARISON BETWEEN CALCITONIN AND CEA RIA IN THE MANAGEMENT OF MEDULLARY THYROID CARCINOMA (MEETING ABSTRACT).

Girelli ME, Busnardo B, Moro A, Simioni N, Scotton G
No affiliation given

Eur J Nucl Med; 6:71 1981

Serum levels of Calcitonin (CT) and Carcino Embyronic Antigen (CEA), were measured by radioimmunoassay in 35 out of a group of 46 patients with Medullary thyroid carcinoma. Sixteen patients were studied before thyroidectomy, and 19 patients only after treatment. In a total of 29 patients CT and CEA levels were repeatly evaluated by serial blood samples over a 1-4 yr period. Before operation 15 of the 16 patients showed elevated CT levels and only 10 showed elevated CEA levels. After operation 58% of the patients showed elevated CT levels and only 31% elevated CEA levels. No patient neither before nor after thyroidectomy showed elevated CEA with normal CT levels. Significant positive correlation between CT and CEA levels was found. Before operation, patients without metastases seem to have had CT and CEA levels less increased than those of patients with local or distant metastases. The difference becomes more evident after treatment. Of the 16 patients without metastases 5 had persistently elevated CT levels and 2 elevated CEA levels. Of the 12 patients with metastases 10 had elevated CT levels and 7 elevated CEA levels. Persistent elevation of CT levels after thyroidectomy in absence of evident metastases, even though CEA levels are normal, probably reflects the presence of minute occult foci of tumor, primary or metastatic. The data suggest that the production of CEA by MCT is less constant and less sensitive than that of CT, which remains the best marker of Medullary thyroid carcinoma. (no Refs)

27. CARCINOEMBRYONIC ANTIGEN (CEA) ACTIVITY IN GASTRIC JUICE IN PATIENTS WITH MALIGNANT AND NON-MALIGNANT DISEASES OF THE STOMACH (MEETING ABSTRACT).

Lemberger J, Novakovic R, Marton B, Libman E, Petronijevic LJ, Glisic LJ
No affiliation given
Eur J Nucl Med; 6:102 1981

The previous studies have shown that the CEA test in blood has a limited diagnostic value in confirming the malignancy of the stomach. We have conducted researches of the CEA activity in the gastric juice of patients with stomach diseases. The simultaneous radioimmunoassay of CEA in the serum and in the gastric juice was done in 18 patients non-malignant diseases and in 17 patients with gastric carcinoma. The mean CEA activity in the gastric juice of patients with non-malignant stomach diseases and with gastric carcinoma is 923 +/-220 ng/ml and 3313 +/-558 ng/ml respectively. The difference is significant (p 0.001). No correlation was found between the CEA activity in the serum and gastric juice. Some dilution curves of the stomach juice are not parallel to the standard curve. This shows that in the course of radioimmunological determination of CEA a cross reaction of the CEA-like substances is evident. Achieved results suggest that in patients with gastric carcinoma an elevated CEA antigenemia persists not only in the blood but in the gastric juice as well. For the evaluation of the diagnostic values of the combined measurement of CEA activity both in the serum and in the gastric juice further research is necessary. (no Refs)

ULTRASTRUCTURE/ CYTOCHEMISTRY

28. THE PRESENCE AND DISTRIBUTION OF CARCINOEMBRYONIC ANTIGEN IN TUMORS OF HUMAN MINOR SALIVARY GLANDS.

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J Oral Pathol; 10(4):296-303 1981

The peroxidase-anti-peroxidase technique was used to investigate the presence and distribution of carcinoembryonic antigen (CEA)-positive tumors in a consecutive series of 62 minor salivary gland tumors from 60 patients (20 males, 40 females; mean age 51.6 yr, range 11-77 yr). Thirty-four (55%) of the tumors gave a positive staining reaction for peroxidase, indicating the presence of CFA or CEA-like material in the neoplastic tissues. With the exception of the monomorphic adenomas, all varieties of tumors studied included some specimens that were positive for CEA: 23/44 adenomas and mucoepidermoid tumors, and 11/18 carcinomas were positive. In 11 tumors, CEA staining was present in many cells or neoplastic ducts, and in 23 tumors it was definite in only a few cells or neoplastic ducts. Positive staining was focally distributed in all but two tumors where it was widely and diffusely distributed. Positive staining for CEA was usually restricted to well-differentiated neoplastic ductal cells, although it was sometimes seen in more primitive ducts. Non-neoplastic acini at the periphery of tumors or in areas of inflammation also showed definite staining. The histologic presence of CEA in a particular tumor may indicate the need for postoperative monitoring of saliva and plasma, particularly where residual tumor, metastases, or recurrences are likely. (12 Refs)

29. A DILUTIONAL IMMUNOPEROXIDASE STUDY OF PROLIFERATIVE DUCTAL LESIONS AND CARCINOMATA OF THE BREAST.

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Histopathology; 5(5):517-526 1981

A dilutional immunoperoxidase technic using antiserum against carcinoembryonic antigen (CEA) was used to differentiate cases of epitheliosis, in situ and infiltrating ductal carcinoma, and in situ and infiltrating lobular carcinomas of the breast. In most of the cases of mild epitheliosis, the highest dilution of glycocalyceal staining was 1/400 and intraluminal staining 1/800. In cases of severe epitheliosis, intracytoplasmic staining, when present, was seen at dilutions of up to 1/400. Adjacent normal acini showed prominent glycocalyceal staining. In intraduct carcinoma cases, with cribriform/clinging patterns, positive staining was present in the following ranges: intracytoplasmic 1/100-1/5,000, glycocalyceal 1/800-1/5,000, and intraluminal 1/200-1/25,600. In all the cases of intraduct carcinoma with cribriform/clinging pattern and solid pattern with infiltration, the intraduct component stained at lower dilutions than the cases of pure intraduct carcinoma. Intraluminal staining was present in lower concentrations in the infiltrating component when compared with the intraduct part of the tumor. Intracytoplasmic staining was seen in the infiltrating component in some cases. In some cases of in situ lobular carcinoma with infiltration, intraluminal staining was noted in foci of adenosis and epitheliosis adjacent to lobular carcinoma. However, the normal breast tissue adjacent to the tumors did not usually stain positively at dilutions greater than 1/50. Results indicated that the dilutional immunoperoxidase technic for CEA appears useful in differentiating cases of severe epitheliosis from cribriform/clinging pattern of intraduct carcinoma. (12 Refs)

30. SERUM AND TISSUE CARCINOEMBRYONIC ANTIGEN IN BENIGN AND MALIGNANT LESIONS OF THE BREAST.

von Kleist S, Wittekind C, Polack M, Gropp H, Sandritter W
Forschergruppe Tumorimmunologie, Institut fur Immunobiologie der Universitat Freiburg, Stephan-Meier-Strasse 8, D-7800 Freiburg i. Br., W. Germany
Arch Geschwulstforsch; 51(6):523-526 1981

The serum (enzyme assay) and tissue (immunoperoxidase test) levels of carcinoembryonic antigen (CEA) were determined in 51 cases of breast cancer and in 33 benign breast lesions. CEA-positive tumors were found to be accompanied by low or negative CEA serum levels. The stage and histologic type of lesions were compared with the positivity and the increase of CEA. (5 Refs) (In FRE)

31. IMMUNOPEROXIDASE LOCALIZATION OF CARCINOEMBRYONIC ANTIGEN IN NORMAL HUMAN INTESTINAL MUCOSA.

Primus FJ, Clark CA, Goldenberg DM
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JNCI; 67(5):1031-1039 1981

The indirect, labeled antibody and peroxidase-antiperoxidase complex (PAP) methods were studied to determine their sensitivity in detecting carcinoembryonic antigen (CEA) in conventionally processed specimens of morphologically normal human colon mucosa. CEA-positive staining was demonstrated in 13 of 19 specimens reacted with the PAP method, whereas only 4 of these specimens stained positive with the labeled antibody procedure. Detection of CEA with either technique was unrelated to normal mucosa content of antigen as determined by radioimmunoassay. Tissue fixation in 95% ethanol-1% acetic acid (EA) resulted in an enhanced and defined cytoplasmic staining of the normal colon cell lining the mucosal surface and upper levels of the glandular crypts. Cytoplasmic localization in Formalin-fixed specimens was absent or markedly reduced. Colon goblet cells and the small intestinal epithelium were CEA-negative in both Formalin- and EA-fixed specimens. These results show that the PAP immunoperoxidase method is more sensitive than the indirect, labeled antibody procedure in detecting CEA in morphologically normal colon mucosa. Furthermore, staining of tissues fixed in EA demonstrated that CEA is a product of the columnar epithelial cell and is not associated with goblet cells. (Author abstract) (38 Refs)

32. TRANSFORMATION ASSOCIATED FETAL ANTIGENS IN HUMAN PREMALIGNANT COLONIC EPITHELIAL CELLS (MEETING ABSTRACT).

Higgins PJ, Friedman E, Lipkin M, Hertz R, Attiyeh F
Memorial Sloan-Kettering Cancer Center, New York, NY, 10021
Gastroenterology; 80(5,part2):1174 1981

Premalignant and malignant colonic cells were analyzed for transformation associated fetal antigens by immunohistologic techniques using rabbit antiserum to combined saline extracts of heart, lung, liver, kidney, spleen and small and large intestine obtained from a 2nd trimester human abortus. Antiserum had been absorbed with extracts of the corresponding adult tissues obtained at autopsy from non-cancer related deaths, and A and B RBC. Immunohistologic studies revealed anti-fetal reactivity in 84% of colonic adenocarcinomas examined by cryostat sectioning, and in all established and short term colon carcinoma cell cultures tested. Normal epithelial cells of the colon did not stain with this anti-serum. Absorption of anti-2nd trimester fetus serum with an established colon carcinoma cell line (SW 1116) removed anti-body to all tumors. Parallel absorptions with extracts of normal colonic tissues were without effect, suggesting that the anti-serum recognizes one or several closely related fetal antigens. Control experiments indicated that the antigen(s) detected was not alpha fetoprotein, beta human chorionic gonadotropin, or carcinoembryonic antigen. Primary cultures of adenomatous colonic epithelial cells were then examined for the presence of fetal antigen. Cultured epithelial cells stained positively in 2 of 11 (18%) tubular adenomas, 3 of 6 (50%) villotubular adenomas, and 5 of 6 (83%) villous adenomas. We conclude that colonic epithelial cells of human adenomas express fetal antigen with increased frequency as they progress through stages towards frank carcinoma. (no Refs)

33. IMMUNOCYTOCHEMICAL EVALUATION OF SKIN METASTASES (MEETING ABSTRACT).

Heyderman E, Gibbons AR, McGibbon DH
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Brit J Dermatol; 105(Suppl19):9 1981

While most deposits of metastatic tumor which are associated with an occult primary site and give rise to diagnostic problems are in lymph nodes, some tumors first present with skin nodules. Using a variety of antisera and an indirect immunoperoxidase technique, we have shown that diagnostic accuracy can be improved by determining whether various antigens are demonstrable in the tumor deposit. Thus we have used antisera to human chorionic gonadotrophin (HCG) to identify atypical deposits of gestational and testicular choriocarcinoma; and to epithelial membrane antigen (EMA) and carcinoembryonic antigen (CEA) to suggest a gastrointestinal or breast origin. By evolving a battery of tissue markers one will be able to offer the clinician a better guide to the possible primary site of an occult tumor than can be achieved by purely morphological examination. (no Refs)

34. MUCIN COMPOSITION AND CEA CONTENT IN ASSESSING MALIGNANT POTENTIAL OF COLONIC ADENOMAS (MEETING ABSTRACT).

Filipe MI, Abbas S, Greaves P
Department of Histopathology, Westminster Medical School, London, England
Eighth European Congress of Pathology, August 30-September 4, 1981, Helsinki, Finland. The Congress 92 pp., 1981.

Adenomas are considered precursors of colo-rectal cancer yet no precise marker exists for assessing their malignant potential. We studied the variations in the composition of mucus secretion and the presence of carcinoembryonic antigen (CEA) in 74 colonic adenomas (from patients with and without synchronous colonic cancer), 22 carcinomas and adjacent 'Transitional' (Tr) mucosa. We found A) as in normal a high proportion of O-acylated sialomucins in 'Tr' mucosa and benign adenomas but its absence in polyps with malignancy and in carcinoma; and B) a progressive increase in CEA from low in 'Tr' mucosa, raising with dysplasia in adenomas to a max in carcinoma. These changes were similar in both incidental and synchronous adenomas and related to dysplasia. All controls, including normal mucosa, 8 inflammatory and 7 metaplastic polyps showed high levels of O-acylated sialomucins and minimal or absent CEA except in the metaplastic polyps where CEA was seen. These changes may be an expression of abnormal maturation or early malignant transformation and prove useful as complement to the histological criteria of premalignancy. Furthermore, they illustrate the progression of change from a pre-adenomatous state to adenoma and malignancy. (no Refs)

35. EMBRYONIC AND PLACENTAL ANTIGENS IN HUMAN TESTICULAR GERM CELL TUMORS (MEETING ABSTRACT).

Damjanov I, Fox N
Department of Pathology and Laboratory Medicine, Hahnemann Medical College and Hospital, Philadelphia, PA
Eighth European Congress of Pathology, August 30-September 4, 1981, Helsinki, Finland. The Congress 92 pp., 1981.

We have studied the distribution of embryonic and placental antigens on the surface of human testicular germ cell tumors. Embryonal carcinoma cell express SSEA-3, an antigenic determinant recognized by monoclonal antibodies raised against early cleavage stage mouse embryos and present normally on follicular eggs, fertilized eggs and early mouse embryos up to the morula stage. Yolk sac elements express SSEA-1, an antigenic determinat recognized by monoclonal antibodies raised against the stem cells of mouse teratocarcinoma and present on the cells of the inner cell mass of the mouse blastocyst, primitive mouse ectodermal cells and mouse primordial germ cells, but not on adult mouse ovarian and testicular germ cells. Antigenic determinants recognized by monoclonal antibodies raised against the human placental alkaline phosphatase were found on trophoblastic elements of the tumors and some but not all embryonal carcinoma cells. Parallel studies performed on mouse teratocarcinomas showed that mouse embryonal carcinoma cells express SSEA-1 but not SSEA-2, and have no

human alkaline phosphatase. These data indicate that stem cells of human germ cell tumors are antigenically polymorphic and not homogeneous, as in the mouse. (no Refs)

REVIEWS/ OTHER RELATED STUDIES

36. ONCOFETAL PROTEINS IN THE DIAGNOSIS OF FETAL MALDEVELOPMENT AND CANCER.

Seppala M

OB-GYN Clinic, Helsinki General Municipal Hosp., 00290 Helsinki 29, Finland

Duodecim; 97(10):12-22 1981

A review is presented of alpha-fetoproteins (AFP), chorionic gonadotropins, and placental protein five with respect to birth defects and cancer. Certain types of cancer of the sex organs have a structure analogous to that of the yolk sac; these cancers can secrete AFP into the blood. Radioactive AFP fed to a patient will produce a tumor 3-5x more radioactive than healthy tissue. Luteinizing hormone (LH) and human chorionic gonadotropin (HCG) contain alpha and beta chains; the alpha chain is identical for both, the beta chains differ. Methods currently under study for radioimmune identification of the beta chain may revolutionize the treatment of placental cancer. Radioimmunoassay can detect the quantity of HCG produced by 10,000 cells; other methods require at least 1 million times as many cells and a tumor diameter of 0.5 cm. Early discovery and treatment of placental cancer permits total patient recovery and subsequent childbearing. Current research is focused on the factors influencing synthesis of HCG and free alpha chains in cancer cells. The synthesis of LH, FSH, and their subunits is thought to be triggered by the LH-releasing hormone (LHRH) of the hypothalamus. LHRH and its subunits have been found in the islets of Langerhans, and with pancreatic cancer, breast cancer, and carcinoids. Breast cancer in rats can be controlled by administration of LHRH-analogues. (40 Refs) (In FIN)

37. TUMOR IMMUNOLOGY II. STUDY OF METHODOLOGY.

Crisci CD

Catedra de Neumonologia, Alergia e Inmunologia Clinica, Facultad de Ciencias Medicas. Universidad Nacional de Rosario, Rosario, Argentina

Rev Fac Cienc Med Univ Nac Rosario; 14(1):34,37-42,45-47 1981

Immunologic diagnostic methods for tumors are reviewed. Topics discussed include tumoral markers (enzymes, hormones, oncofetal antigens), immunocellular system (lymphocyte subpopulations, their functional and characteristic differences, identification of lymphocyte subpopulations, exploration of lymphocyte functions), and specific antitumoral response (methods in vitro and in vivo). Systematic study with periodic determinations during many yr may make possible evaluation of the effect of different therapies on a patient's immunological system. (no Refs) (In SPA)

38. THE EXPANDING FIELD OF COLORECTAL CANCER MARKERS: CEA, THE PROTOTYPE.

Zamcheck N

Mallory Gastrointestinal Res. Lab., Boston City Hosp., Boston, MA

Cancer Bull; 33(4):141-151 1981

Carcinoembryonic antigen (CEA) is the sole established marker for colorectal cancer. CEA is not specific to colorectal cancer or to cancer in general. CEA measurements appear to monitor experimentally induced changes in cultured human colon cancer cells just as they monitor changes in a patient's clinical course. Several molecules similar to CEA exist. Non-CEA-like antigens are increasing in number. The use of serial CEA determinations is the principal method for following a patient's clinical course, serves as one indication of successful or incomplete resection of colorectal cancer, gives evidence of recurrence, is useful in monitoring the effect of chemotherapy or radiation therapy and in decision-making to alter therapy, and provides a useful estimate of prognosis. Plasma CEA level provides a useful but not absolutely quantitative index of tumor mass and spread. Variability in plasma CEA levels is a result of many factors, including the marked variation in CEA produced by colonic tumor cells and in the amounts produced by primary colon cancer and metastases. The role of the liver in regulating CEA levels is discussed. Histopathologic evidence of tissue CEA production by positive tissue immunofluorescence or immunoperoxidase staining is regularly found in well-differentiated colorectal adenocarcinomas. Other topics discussed include tissue differentiation and preoperative CEA levels in prognosis and stratification, CEA activity in other body fluids, radioimmunodiagnosis, thermolabile polypeptide of CEA, serum galactosyltransferase isoenzyme, colon mucoprotein antigens, zinc glycinate marker, and combinations of markers. (140 Refs)

39. THE ROLE OF RECEPTORS IN HORMONE MEDIATED REGULATION OF ALKALINE PHOSPHATASE IN CULTURED HUMAN CANCER CELLS (HELA) (MEETING ABSTRACT).

Antonopoulos PA, Singer RM

Department of Anatomy, Fairleigh Dickinson University School of Dentistry, Hackensack, NJ

Anat Rec; 199(3):12A 1981

HeLa cells have been cloned into two sublines monophenotypic for alkaline phosphatase. HeLa TCRC-1 cell line produced a placental alkaline phosphatase while the HeLA TCRC-2 cell alkaline phosphatase was most similar to the bone/liver type. Our studies on regulation of enzyme activity have indicated that glucocorticoid hormones (Prednisolone) enhanced the activity of alkaline phosphastase in the Regan producing HeLa TCRC-1 cell line while the non-Regan producing HeLa TCRC-2 cell line was unaffected in this respect. This difference of gene expression of the carcinoplacental isoenzyme of the HeLa sublines provides a model with which to further study hormonal regulation of gene expression. We shall report our data on the HeLa cell sublines, TCRC-1 and TCRC-2 with respect to the number of hormonal receptor sites for prednisolone in both the cytoplasmic and nuclear fractions. The mechanism of hormone action on the levels of enzyme activity can be at the gene level directly, or a receptor mediated phenomenon. To this end, we have assayed for the levels of hormone receptors in these two HeLa sublines using a tritium ligand binding method. This method relies on the detection of bound tritium labelled steroid. Free unbound steroid is absorbed using a dextran coated charcoal. (no Refs)

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STRUCTURE/ IDENTIFICATION/ CHARACTERIZATION

1. INTESTINE-ASSOCIATED ANTIGENS IN OVARIAN TUMOURS: AN IMMUNOHISTOLOGICAL STUDY.

de Boer WG, Ma J, Nayman J
Dept. Lab. Medicine, Royal Southern Memorial Hosp., Caulfield South, Victoria 3162, Australia
Pathology; 13(3):547-555 1981

The presence of three intestine-associated antigens, small intestine mucin antigen (SIMA), large intestine mucin antigen (LIMA) and carcinoembryonic antigen (CEA) was studied in the female genital tract and ovarian tumors by immunofluorescence. These antigens could not be detected in normal ovary, benign cysts of ovary, fallopian tube or endometrium, but both LIMA and CEA were present in endocervical glandular tissue. The antigenic cross-reactivity of endocervical and large bowel mucin may indicate a close embryological relationship between these organs during the cloacogenic stage. The three antigens could be demonstrated in mucinous tumors of the ovary but were absent in serous or mesonephroid tumors. In one of the two endometroid tumors CEA was the only detectable antigen.

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These observations confirm the presence of intestinal type of epithelium in cystic mucinous tumors of the ovary and explain the cross-reactivity of mucin of benign tumors of the ovary and mucin from colonic cancer, normal colonic mucosa and gastric mucosa as reported by earlier workers. In the process of malignant transformation the columnar epithelium of ovarian cystadenoma seems to behave in the same way as superficial gastric and gallbladder epithelium by forming inappropriate intestine-associated mucin substances. Our technique may provide a specific means for studies on the histogenesis of female genital tract tumors, particularly ovarian tumors. It can also be used in differentiating between benign and malignant variants of these tumors. (Author abstract) (15 Refs)

2. CHARACTERIZATION OF COLONIC TUMORS WITH DIFFERENT BIOLOGICAL PROPERTIES (MEETING ABSTRACT).

Brattain MG
Department of Biochemistry, University of Alabama in Birmingham, Birmingham, AL, 35294
Oncodev Biol Med; AbstractsBook,1:P4 1981

We have utilized mouse embryo C3H IOT1/2 fibroblasts as feeder layers for the establishment of human colonic cancers with different biological properties in tissue culture. Tissue culture of specimens with and without feeder layers of confluent C3H IOT1/2 cells were compared. In a series of 29 different tumor specimens, 21 long-term cultures of human colonic carcinoma were obtained with feeder layers. From the same set of specimens, only 3 long-term cultures were established in the absence of feeder layers. Analysis of lactate dehydrogenase and glucose-6-phosphate dehydrogenase isoenzyme patterns indicated that transformed C3H IOT1/2 lines developed from the attempted culture of 2 of the 29 specimens. Human cell lines where characterized for their ability to form tumors in nude mice, histology of the resultant tumor, morphology of growth in vitro, growth in semisolid medium and production of carcinoembryonic antigen (CEA). The tumors could be divided into 3 groups on the basis of tumorigenicity in nude mice. Highly tumorigenic lines grew well in semi-solid medium, generally produced undifferentiated tumors and secreted low amounts of CEA in culture. Weakly tumorigenic lines produced differentiated tumors in nude mice and showed little or no growth in semi-solid medium. The third group of lines was non-tumorigenic in nude mice and did not grow in semi-solid medium. However, this group secreted a minimum of 4-12 fold more CEA in culture (at least 150 ng/ml of medium) and had a more epithelial type of morphology than the other two groups. (no Refs)

3. CONCANAVALIN A-AFFINITY HETEROGENEITY OF AFP SECRETED BY RAT YOLK SAC TUMORS (MEETING ABSTRACT).

Smith CJ, Kelleher PC, Sobis H, Vandeputte M
Department of Medicine, University of Vermont, Burlington, VT, 05405
Oncodev Biol Med; AbstractsBook,1:31 1981

Alpha-fetoprotein (AFP) glycosylation as characterized by concanavalin A (ConA)-binding differs among animal species and among different cell types of a single species. Rat AFP glycosylation varies during normal growth, chemical hepatocarcinogenesis and hepatoma growth. To determine the characteristics of AFP glycosylation by a second type of malignancy, 11 AFP-secreting rat yolk sac tumors (YST) were investigated. Four YST were induced by fetectomy and injection of murine sarcoma virus (MSV), 6 YST were induced by fetectomy alone and one YST was induced by implantation of a syngeneic embryo under the kidney capsule without MSV. AFP ConA-binding was determined by affinity chromatography. There was no difference in AFP ConA-binding between the tumor-bearing rats with and without MSV treatment. The percentages of ConA-nonbinding AFP in the serum or ascites fluid of YST-bearing rats were normally distributed and were different from that associated with chemically-induced primary hepatomas. There was no significant difference between the ConA-binding of AFP secreted by YST and either AFP present in amniotic fluid between days 13 and 21 of gestation or AFP in fetal rat serum between days 14 and 19 of gestation. There was a highly significant difference between YST AFP and fetal rat serum AFP following day 19. These results indicate that glycosylation of AFP by these malignant yolk sac cells resembles glycosylation of AFP by normal yolk sac cells. In contrast, glycosylation of AFP by hepatoma cells has no obvious relationship to AFP glycosylation by nonmalignant liver cells. (no Refs)

4. THE PURIFICATION OF HUMAN EMBRYONIC PREALBUMIN (MEETING ABSTRACT).

Page M, Tatarinov YS, Kalashnikov VV
Department of Biochemistry, Universite Laval, Quebec, Canada
Oncodev Biol Med; AbstractsBook,1:45 1981

Human embryonic prealbumin (EPA-1), a glycoprotein present in amniotic fluid, fetal tissue and in various soft tissue tumors was purified and characterized from early amniotic fluid. After an acid extraction, the EPA-1 positive material was separated by hollow fiber ultrafiltration, affinity chromatography on Affi Gel Blue and ion exchange chromatography on diethylaminoethanol Affi Gel Blue. The last traces of impurities were removed by ampholyte displacement chromatography. EPA-1 was found pure by high pressure liquid chromatography on a TSK-3000 column, gel electrophoresis, immunoelectrophoresis and double immunodiffusion. Very low titers of EPA-1 were found in normal serum. Elevated levels were observed in the serum of patients with soft tissue, brain and gastrointestinal cancers. (no Refs)

ASSAY PROCEDURES/ SYNTHESIS

5. APPLICATION OF MONOCLONAL ANTIBODIES TO PURIFIED CEA IN CLINICAL RADIOIMMUNOASSAY OF HUMAN SERUM.

Rogers GT, Rawlins GA, Keep PA, Cooper EH, Bagshawe KD
Dept. Medical Oncology, Charing Cross Hosp., London W6 8RF, England
Br J Cancer; 44(3):371-380 1981

Double-antibody radioimmunoassay using a mouse monoclonal anti-CEA (MA/1) has been used to measure CEA in human serum. Low levels of MA/1-binding CEA have been found in serum from normal individuals and moderately raised levels are sometimes associated with certain non-malignant diseases. As with conventional anti-CEA, the MA/1 antibodies can recognize significant amounts of CEA in serum from patients with a variety of solid tumors. However they appear to recognize a different immunodeterminant and possibly a different population of CEA molecules to, or a subset of, those measured by two routine assays. Studies in which the MA/1 assay was directly compared with the results of the Charing

Cross routine and Abbott EIA assays have indicated that different immunological forms of CEA may be expressed in the course of tumor progression but no prognostic value was evident in this study. Our results stress the need to resolve immunological specificities expressed by CEA-like molecules and evaluate their clinical importance. (Author abstract) (16 Refs)

6. A SPECIFIC RADIOIMMUNOASSAY FOR CARCINOEMBRYONIC ANTIGEN IN MEDULLARY CARCINOMA OF THE THYROID (MEETING ABSTRACT).

Jullienne A, Calmettes C, Moukhtar MS, Taboulet J, Milhaud G

Service de Biophysique, INSERM U113, 27 Rue Chaligny, 75012 Paris, France

Oncodev Biol Med; AbstractsBook,1:27 1981

Medullary carcinoma of the thyroid (MCT) is a calcitonin secreting tumor which we and others have shown to be characterized by high levels of carcinoembryonic antigen (CEA) in tissues and plasma using radioimmunoassays (RIA) specific for CEA extracted from colonic tumors. CEA of MCT origin shows complete cross reaction in this system. We have developed a specific RIA for CEA of MCT origin. Antigen from MCT was purified by a combination of Sephacryl S300 chromatography, concanavalin A affinity chromatography. Antibodies were obtained in the rabbit by immunization of the purified product. The antibodies show a high degree of cross reaction with CEA of colonic antigen, confirming the high degree of homology in the antigenic sites of the two molecules. The radioimmunoassay developed had a sensitivity of 5 ng/ml and a final antibody titer of 1/18000. (no Refs)

7. ROLE OF CEA RADIOIMMUNODETECTION IN THE MANAGEMENT OF COLORECTAL CANCER (MEETING ABSTRACT).

Goldenberg DM, Kim EE, Deland FH, Bennett SJ

Division of Experimental Pathology, University of Kentucky, Lexington, KY, 40536

Oncodev Biol Med; AbstractsBook,1:P62 1981

Radioactive antibodies to carcinoembryonic antigen (CEA) have been shown to detect and locate CEA-producing tumors in man by the method of radioimmunodetection. Although this method is still rapidly developing and improving, clinical advantages have been attained in a number of patients in whom tumor recurrence or metastasis was suspected. Over 52 patients with a history of confirmed colorectal cancer received an iv injection of between 1 and 2.5 mCi of 131-I-labeled, affinity-purified, goat antibody IgG against CEA, followed by total-body photoscanning. Blood-pool and non-target sites or radioactivity were reduced by subtracting the images derived by injection of 99m-technetium components from the 131-I scans. In 10 of the 52 patients, sites of occult cancer could be located and then confirmed by surgery or other methods when, prior to radioimmunodetection, standard detection measures failed to reveal these sites. Elevated CEA plasma levels did not hinder successful tumor detection. It is concluded that cancer radioimmunodetection with highly purified antibodies to CEA is a useful procedure for pre- and post-operative evaluation of patients with CEA-producing colorectal cancer, sometimes revealing sites of tumor not disclosed by other procedures. (no Refs)

8. UTILIZATION OF MONOCLONAL ANTIBODY IN A SOLID PHASE IMMUNOASSAY FOR CEA (MEETING ABSTRACT).

Ulrich T, Tribby I, George S, Tomita J
Abbott Laboratories, North Chicago, IL, 60064
Oncodev Biol Med; AbstractsBook,1:28 1981

A series of fusion experiments using spleen cells from mice immunized with purified carcinoembryonic antigen (CEA) and mouse myeloma cell line P3 or SP2/0 has resulted in several stable hybridomas producing monoclonal antibody with CEA binding activity. Analysis of monoclonal antibody preparations resulting from each fusion indicated that 10-50% of the hybridomas obtained were producing antibody which bound to non-specific cross-reacting antigen as well as CEA. Several CEA specific hybridomas were propagated in mice and the ascites fluids purified by protein A Sepharose affinity chromatography. Yields of purified antibody protein ranged from 3-15 mg/ml of ascites fluid. Affinity constants of these antibodies studied were in the range of 10(9) to 10(10) liters/mole by Sip's analysis. Four CEA specific binding sites were identified by the use of monoclonal antibodies. Antibodies thus characterized were tested for their efficacy in coating polystyrene beads. Using monoclonal antibody in place of guinea pig antibody for coating beads in the present Abbott enzyme immunoassay resulted in nearly identical standard curves. Accordingly CEA values obtained on serum specimens including normals and patient sera by the monoclonal antibody system show greater than or equal to 99% correlation with present Abbott enzyme immunoassay. (no Refs)

9. FALSE-POSITIVE AND FALSE-NEGATIVE ALPHA-FETO PROTEIN AND HUMAN CHORIONIC GONADOTROPIN ASSAYS IN TESTICULAR CANCER: A DOUBLE BLIND STUDY.

Javadpour N, Soares T
Surgery Branch, NCI, NIH, Bethesda, MD, 20205
Cancer; 48(10):2279-2281 1981

The rates of false-positive and false-negative serum alpha-feto protein (AFP) and human chorionic gonadotropin (HCG) determinations in 50 patients with testicular cancer utilizing assays from a reference laboratory were studied. Seven (14%) of 50 patients had false-positive and 1 (2%) of 50 had false-negative serum HCG determinations. Although 6 (12%) of 50 of serum AFP determinations showed false-positive results; no false-negative rates were encountered for serum AFP. Utilizing simultaneous measurements of serum HCG and luteinizing hormone (LH) measuring urinary HCG by a highly specific carboxyl-terminal assay, one may rule out false-positive occurrences of serum HCG in patients with testicular cancer. This double-blind study also confirmed the need for correlating the clinical status of the patients with elevated serum AFP or HCG in patients with testicular cancer before embarking on any therapy. (Author abstract) (6 Refs)

10. IMMUNOPEROXIDASE STAINING FOR CARCINOEMBRYONIC ANTIGEN IN SMALL CELL CARCINOMA OF THE LUNG.

Sehested M, Hirsch FR, Hou-Jensen K
Dept. Pathological Anatomy, Herlev Hosp., Univ. Copenhagen, DK-2730 Herlev, Denmark
Eur J Cancer Clin Oncol; 17(10):1125-1131 1981

Diagnostic pretreatment biopsies in 53 patients with small cell carcinoma of the lung (SCCL) were examined retrospectively for presence of carcinoembryonic antigen (CEA). The unlabeled antibody-enzyme (PAP) technique was utilized. All patients had been treated with intensive chemotherapy. The patients were divided into three groups according to the immunoperoxidase staining reactions of the biopsies. Thirteen (24.5%) patients had biopsies that were strongly positive for CEA while 22 (41.5%) had slightly positive and 18 (34%) had negative biopsies. The patients with biopsies strongly positive for CEA had a significantly longer survival as compared with patients with negative staining results (p less than 0.05). No significant correlation was observed between immunoperoxidase staining for CEA and morphological subtypes of SCCL according to the WHO 1977 classification. (Author abstract) (15 Refs)

EXPERIMENTS IN ANIMAL SYSTEMS

11. RELATIONSHIP OF SERUM CEA LEVELS TO TUMOUR SIZE AND CEA CONTENT IN NUDE MICE BEARING COLONIC-TUMOUR XENOGRAFTS.

Lewis JC, Keep PA
Dept. Medical Oncology, Charing Cross Hosp., Fulham Palace Road, London, England
Br J Cancer; 44(3):381-387 1981

The relationship of serum carcinoembryonic antigen (CEA) levels to tumor size and antigen content was studied in nude mice bearing well differentiated, mucinous human colonic-tumor xenografts. Blood samples were taken from normal nude mice and others bearing xenografts, whose size had been calculated from in vivo measurements; saline and KCl extracts were made of a proportion of these tumors. Sera and tissue extracts were assayed for CEA activity by double-antibody radioimmunoassay. Extracts were also made from the livers and spleens of tumor-bearing and normal nude mice. All normal sera and 78% of sera from tumor-bearing animals had CEA values less than 11.4 ng/ml. No clear correlation was found between serum CEA levels greater than 11.4 ng/ml and tumor size or wt, or between serum CEA and tumor CEA concentrations or total CEA burden. The concentration of CEA in those tumors tested varied from 1 to 22 ug/g. Our results confirm and extend the conclusions reached by others studying the significance of serum CEA levels with xenograft model systems. The complexity of factors contributing to circulating CEA is discussed in the light of our findings. (Author abstract) (39 Refs)

12. ALPHA-FETOPROTEIN: CELLULAR ORIGIN OF A BIOLOGICAL MARKER IN RAT LIVER UNDER VARIOUS EXPERIMENTAL CONDITIONS.

Kuhlmann WD
Lab. Experimental Medicine and Immunocytochemistry, Institut fur Nuklearmedizin, D.K.F.Z., D-6900 Heidelberg, W. Germany
Virchows Arch [Pathol Anat]; 393(1):9-26 1981

Alpha1-fetoprotein (AFP) was detected by serological, light and electron microscopic methods in various experimental models. These included (a) liver regeneration after partial hepatectomy or CCl4 intoxication (mouse and rat); (b) liver intoxication by high doses of N-nitrosomorpholine (NNM) and chemical induction of hepatomas (rat). AFP levels varied greatly according to the animal species and strains used. Low and high AFP-producing species and strains were distinguished. In liver regeneration after hepatectomy or CCl4 intoxication, cellular AFP was found in the cytoplasm of hepatocytes. In NNM-intoxicated livers, elevated AFP levels were associated with proliferation of canalicular epithelial cells in which AFP was localized. In early stages of hepatocarcinogenesis, significant AFP increase occurred after high-dose carcinogen feeding and AFP was also localized in proliferating canalicular epithelial cells. On low-dose NNM feeding, no cellular AFP was detected unless hepatomas had developed. At the stage of malignant conversion, distinct AFP staining and non-AFP staining hepatocellular carcinomas appeared in livers. (Author abstract) (69 Refs)

13. VIRAL VERSUS NON-VIRAL INDUCED YOLK SAC TUMORS IN THE RAT (MEETING ABSTRACT).

Sobis H, Van Hove L, Vandeputte M
Rega Institute, University of Leuven, Leuven, Belgium
Oncodev Biol Med; AbstractsBook,1:40 1981

Yolk sac tumors were induced in fetectomized rats by displacement of the visceral yolk sac outside the uterus with or without injection of Murine Sarcoma Virus (MSV) into the placenta. Some of the animals were immunized with MSV prior to surgery. The biological, morphological and immunological characteristics of the tumors which developed in animals injected or not with virus were compared. The results clearly indicate that MSV inoculation into the placentas of fetectomized rats plays a definite role in the induction of visceral yolk sac derived malignant tumors. This conclusion is based on the following findings: (1) the tumor incidence is significantly greater in the MSV-inoculated group; (2) the latency period is markedly shortened; (3) all the early tumors in the virus group appeared in the MSV-inoculated horn; (4) in the groups preimmunized with MSV the results were quite similar to those recorded in the rats treated with fetectomy alone; (5) only in the virus group did we observe the development of less differentiated tumors (embryonal carcinomas). The transplanted and/or in vitro cultured yolk sac carcinomas derived from primary tumors obtained in animals injected or not with MSV show the same morphology, are not immunogenic, secrete alpha-fetoprotein and express endodermal antigen. (no Refs)

14. SELECTIVE REMOVAL OF AFP FROM SERA OF HEPATOMA-BEARING RAT BY EXTRACORPOREAL CIRCULATION (MEETING ABSTRACT).

Kanai K, Nakajima T, Morioka S, Kako M, Sato N, Kiyota T, Hayashi H
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Oncodev Biol Med; AbstractsBook,1:P5 1981

An extracorporeal circulation system consisting of plasma separator (cellulose acetate hollow fiber, 330nm in diameter) and anti-alpha fetoprotein affinity column (capacity, 300ug AFP/cm3 column) which could efficiently remove AFP from the sera of hepatoma-bearing rats was developed in an attempt to elucidate the biological significance of AFP in tumor-bearing animals. Blood was taken from femoral artery of the rat, led into the circulation system and finally returned to femoral vein. This procedure was repeated several x hr each rat. About 70% of AFP was removed from sera after 4 hr of circulation when 30ml of fresh rat blood which contained 12ug/ml of AFP was used in the system. Disc electrophoresis revealed that AFP was the only protein retained on the affinity column. A remarkable decrease of serum AFP was seen after each circulation. However, decreased AFP returned to the previous level several days after circulation perhaps reflecting rapid growth of the tumor, although serum AFP level of the experimental group tended to remain low compared with that of control group. (no Refs)

15. GUINEA-PIG AFP DURING NORMAL ONTOGENESIS, LIVER CARCINOGENESIS, AND UNDER HORMONE TREATMENTS (MEETING ABSTRACT).

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Oncodev Biol Med; AbstractsBook,1:P6 1981

Guinea-pig alpha fetoprotein (AFP) was purified to homogeneity, characterized, and a radioimmunoassay was developed. Serum AFP level in fetal guinea-pig remains in the mg/ml range up to the 8th gestational wk and then drops rapidly. The electrophoretic and lectin affinity molecular variants of AFP change during ontogenesis, probably in relation with changes in carbohydrate composition of the protein. The liver and the yolk sac are the main sites of AFP synthesis during fetal life with the stomach and the small intestine contributing smaller amounts, as measured by peptide pulse labeling assays in vivo. Compared to other species, serum AFP levels are very high in normal adult guinea-pig; these levels are reduced dramatically by administration of glucocorticoids or ACTH. The hormone effect is rapidly reversed upon withdrawal. In guinea-pigs fed with diethylnitrosamine, serum AFP increases at the time liver tumors appear; there is no early induction and the increase is much less than in rats under similar treatment. (no Refs)

16. CORRELATION OF GROWTH OF HUMAN TUMOR CELL LINES WITH CIRCULATING CEA IN NUDE MICE (MEETING ABSTRACT).

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Oncodev Biol Med; AbstractsBook,1:25 1981

Two sublines of a human secondary colonic cancer (SL), and two sublines of HT 29 cells each with a different in vitro secretion rate of carcinoembryonic antigen (CEA) were inoculated sc into nude mice. Tumor growth was estimated by measuring the diameters of a tumor as well as by determining the wt of the excised tumor. Serum CEA was determined with the CEA-Roche-radioimmunoassay-test kit using the indirect method. Up to 30 days after inoculation of tumor cells exponential increases were observed for the serum CEA concentration, tumor wt and tumor vol. The correlation coefficient for increases in CEA and tumor wt was 0.97 and for increases in CEA and tumor vol 0.92. Prolonged observation up to 60 days frequently revealed diminished CEA increases, sometimes CEA decreases, and correlation with tumor wt and vol became less significant. Preliminary histologic investigations indicated that necrosis of the tumor could be a potential factor for this phenomenon. (no Refs)

17. THE DISTRIBUTION OF PARENTERALLY ADMINISTERED ANTIBODY TO CEA IN COLO-RECTAL XENOGRAFTS (MEETING ABSTRACT).

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Oncodev Biol Med; AbstractsBook,1:25 1981

Autoradiography was used to identify the distribution of parenterally administered anti-carcinoembryonic antigen (CEA) in human colo-rectal tumors xenografted to nude mice. Four xenograft lines were studied: Three mucinous adenocarcinomas of various degrees of differentiation and one anaplastic tumor. Affinity purified goat antiCEA labelled with 125 Iodine was given intravenously to xenograft bearing nude mice. At various x after administration (max 7 days), autoradiograms were prepared for 5 micron tumor sections by a modified Appleton diffusible compound technique and by conventional methods. The experiments were duplicated using a nonspecific goat gamma globulin. By combining autoradiography with a PAP immunoperoxidase method of demonstrating CEA, antiCEA was found to be preferentially retained at sites of CEA positive necrotic debris and extracellular collections of CEA positive eosinophilic material within mucinous areas. Cell surface retention was not observed. At most x following administration more antibody was detected within extracellular mucin and stromal connective tissue than within the tumor cell compartment. These studies are being followed by further experiments using monoclonal antibodies to aid design of antibody-drug conjugates for tumor therapy. (no Refs)

18. RELEASE OF CEA FROM HUMAN COLONIC CARCINOMAS GRAFTED INTO NUDE MICE: ARE THERE NON SECRETOR TUMORS? (MEETING ABSTRACT).

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Institut fur Immunbiologie, Freiburg, W. Germany
Oncodev Biol Med; AbstractsBook,1:26 1981

The close correlation between the tumor stage (total tumor burden) and carcinoembryonic antigen (CEA) serum concentration has long been established in colorectal cancer patients, yet even in these carcinomas it never reaches 100%. In other tumors, eg of the breast, this relationship is much worse: Only 30-40% of N+ and 56-72% of N+, M+ patients have elevated CEA-serum levels despite the fact that their tumors are CEA positive. We postulated that nearly all carcinomatous tissues produce CEA but not all malignant cells release it equally well. In order to further prove our point, 50 nude mice were transplanted with 9 different human colon tumor fragments of initially equal size and similar histology. Serial CEA determinations in the mice demonstrated a close correlation between log tumor vol and log CEA values. Xenografts of patients with normal serum CEA levels even when distant metastases were present, yielded near normal CEA in the serum of the nude mice. This suggests that there might be, indeed, 'non-secretor' tumors, since, even in an identical environment these tumors, although growing, did not release the CEA they contained, as shown by immunohistology, while other CEA positive tumors did. (no Refs)

19. SURVEY OF SPONTANEOUS AND CARCINOGEN-INDUCED RODENT TUMORS FOR GAMMA FETAL ANTIGEN (MEETING ABSTRACT).

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Oncodev Biol Med; AbstractsBook,1:47 1981

Previous studies revealed the presence of a 35,000 dalton gamma-migrating antigen in saline extracts of several mouse fibrosarcomas and hepatic carcinomas. This antigen was designated gamma-fetal antigen (gamma-FA) since it possessed gamma electrophoretic mobility and could be extracted from late-gestation mouse fetuses. To determine the extent to which gamma-FA is associated with spontaneous and carcinogen-induced murine cancers, neoplasms representing 12 different tissue sites of origin were examined serologically. Gamma-FA was identified in 17 of 23 such tumors with malignancies of neural ectoderm generally constituting the gamma-FA-negative class. Mice bearing gamma-FA-positive tumors had detectable levels of gamma-FA in their sera. Immunochemical and physico-chemical analysis of gamma-FA extracted from several histologically distinct tumor types indicated that the antigen detected in each case was indeed gamma-FA. The occurrence of gamma-FA in 75% of the malignant tumors examined, its presence in the sera of mice bearing transplanted and primary cancers and the absence of this antigen in the serum of normal mice suggests an associative relationship of potential diagnostic value. This possibility is supported by the observation that immunoprecipitable gamma-FA appeared in the sera of hepatocarcinogen-treated rats several wk prior to the initial detection of alpha-fetoprotein. (no Refs)

20. BLOOD ALPHA-FETOPROTEIN CHANGES IN RATS FED AFLATOXIN B1 AND VARIOUS LEVELS OF CABBAGE.

Boyd JN, Stoewsand GS
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J Food Sci; 46(6):1923-1926 1981

Weanling male Fischer rats were fed semi-purified diets containing 0, 5, 10, 20 or 30% freeze-dried ground cabbage for 11 wk. 'Control' groups received no aflatoxin B1 (AB1), 'Ad lib AB1' groups received 1 ppm AB1 in the diets, and 'Meal-fed AB1' groups received two weekly 'meals' of AB1 in 3-5g of purified diet. The amounts of AB1 consumed per wk were the same for both AB1 treated groups. Blood levels of alpha-fetoprotein (AFP), an onco-developmental gene product, were in the order: 'Meal-fed AB1' greater than 'Ad-lib AB1' greater than 'Control'. Inhibition of AFP elevation by cabbage diets in both AB1-treated groups suggested that this vegetable may produce a hepatocarcinogenic protective effect. This effect has been observed in rats fed cauliflower. Inhibition of AFP induction was correlated with increasing levels of dietary cabbage up to 20%. Cabbage diets also resulted in decreased intestinal transmit time and increased relative liver wt. (Author abstract) (25 Refs)

21. RAT ALPHA-FETOPROTEIN IS NOT PRODUCED CONSTITUTIVELY IN MOUSE HEPATOMA X NORMAL ADULT RAT HEPATOCYTES HYBRIDS, NOR IS IT INDUCIBLE BY ETHIONINE TREATMENT (MEETING ABSTRACT).

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Genetic Laboratory, Free University of Brussels, Rhode-St-Genese, Belgium
Oncodev Biol Med; AbstractsBook,1:P7 1981

We have previously reported that hepatocyte hybridomas can be generated by fusing mouse hepatoma cells with hepatocytes from normal adult rat; such hybrids segregate rat chromosomes, but retain the capacity to secrete one or several rat serum proteins like the normal hepatocyte parent. They actively secrete mouse alpha fetoprotein (AFP), like the parental mouse hepatoma cells, but do not produce rat AFP in sizeable amount. We have now isolated new hybrids clones which differ from the previous ones in having retained a high number of rat chromosomes; however, like the previous hybrids, they do not secrete rat AFP in amount detectable by radioimmunoassay. No stimulation of AFP production could be observed by treating hybrid cells with ethionine, a hepatocarcinogen known to activate AFP production in vivo. In these hybrids, the rat AFP genes, contributed by the adult hepatocyte are thus not activated, although they co-exist with active mouse AFP genes. In the course of this study, we also found that rat hepatoma lines derived from the Reuber H35 hepatoma secrete low amounts of rat AFP; their rate of AFP secretion changes during the growth cycle (it is decreased during the stationary phase), and is not stimulated by ethionine treatment, or by hybridization with AFP-producing mouse hepatoma cells. (no Refs)

22. APPLICATION TO BENZO(A)PYRENE FED RATS OF A PROPOSED SHORT-TERM IN VIVO CARCINOGEN SCREENING PROTOCOL (MEETING ABSTRACT).

Boyd JN, Misslbeck N, Campbell TC, Babish JG, Stoewsand GS
Department of Preventive Medicine, Cornell University, Ithaca, NY
Toxicologist; 1(1):36 1981

This study was undertaken to determine if induction of presumptive pre-cancerous lesions by benzo(a)pyrene (BP) could be predicted in a short-term treatment by demonstration of urinary mutagenesis and by increased concentration in the blood of the oncodevelopmental protein alpha fetoprotein (AFP). Existence of pre-cancerous lesions was confirmed by gamma glutamyl transpeptidase staining of liver sections from treated animals. Male weanling F344 Schf rats were fed semi-purified diets containing 0, 1, 100 or 1000 ppm BP with or without 0.05% sodium phenobarbital for six to thirteen wk. Blood was obtained at one to two wk intervals by cardiac puncture and plasma AFP levels were determined by sandwich type radioimmunoassay. Urine was collected for eight hr during the sixth wk of treatment. Glucuronidase-treated specimens were tested for mutagenesis in salmonella typhimurium strains TA98 and TA100 with and without microsomal activation. Liver specimens were stained for gamma glutamyl transpeptidase (GGT) activity and examined for presence of foci of altered cells. Those treatments resulting in elevated plasma AFP and mutagenic urine were associated with development of GGT-positive hepatic cell foci. This protocol could be applied ea rly in the range finding phase of a carcinogenesis bio-assay to aid in selection of substances for long-term testing. (no Refs)

23. INDEPENDENCE OF ALPHA-FETOPROTEIN EXPRESSION FROM SERUM PROTEIN PRODUCTION IN ADULT RATS BEARING HEPATOMA MCA-RH7777.

Abelev GI, El'gort DA, Eraizer TL
Lab. Immunochemistry and Tumor Diagnosis, All-Union Cancer Res. Center, Moscow, USSR
Biull Eksp Biol Med; 91(9):333-335 1981

Regulation of alpha-fetoprotein (a-FP) expression was studied in cells of cultured rat hepatoma McA-RH7777. Comparison of clones with the highest and lowest a-FP concentrations showed that a-FP expression did not depend upon the synthesis of other adult serum protein by the tumor cells. (8 Refs) (In RUS)

24. EXPRESSION OF HUMAN FETAL BRAIN ANTIGENS BY HUMAN TUMORS OF NEUROECTODERMAL ORIGIN AS DEFINED BY MONOCLONAL ANTIBODIES.

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Cancer Res; 42(1):267-275 1982

The antigenic relationships between human tumors of neuroectodermal origin and fetal brain were investigated by the production of hybridoma antibodies derived from a fusion of P3-NS1/1-Ag 4-1 (NS1) myeloma cells with splenocytes from a mouse multiply immunized with a homogenate of second-trimester human fetal brain tissue. Two monoclonal antibodies (MAs), 4D2cl 6 and 7H10cl 4, were studied in detail by cell surface radioimmunoassay (CS-RIA), quantitative absorption, indirect immunofluorescence, and peroxidase-anti-peroxidase (PAP) immunohistology. MA 4D2cl 6 binds to 5 of 14 glioblastoma (GBM) cell lines, 1 of 2 melanoma cell lines, 1 of 3 neuroblastoma cell lines, and 1 of 5 fetal fibroblast lines by CS-RIA and to 13 of 13 GBM, 1 neuroblastoma, and fetal brain, liver, spleen, and adult spleen unfixed frozen tissue by PAP analysis. MA 7H10cl 4 binds to 13 of 14 GBM, 1 of 3 neuroblastoma, and 1 medulloblastoma cell line(s) by CS-RIA analysis and to 13 of 13 GBM, 1 neuroblastoma, fetal brain, liver, spleen, thymus, and adult spleen by PAP analysis. Control non-CNS tumors and normal adult tissue, including brain, were unreactive with both MAs by CS-RIA, PAP, and absorption analysis. Tissue distribution and localization analyses established that MAs 4D2cl 6 and 7H10cl 4 recognize specificities of shared fetal-neuroectodermal-lymphoid distribution which are operationally specific within the adult CNS and which are not related to previously described oncofetal or onconeural antigens. (Author abstract) (36 Refs)

25. USE OF AN AGAR CULTURE TECHNIQUE FOR ESTABLISHING LYMPHOID CELL LINES FROM MAREK'S DISEASE LYMPHOMAS.

Payne LN, Howes K, Rennie M, Bumstead JM, Kidd AW
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Int J Cancer; 28(6):757-766 1981

Lymphoblastoid cell lines derived from Marek's disease (MD) lymphomas have been established with difficulty by a number of workers. We have compared with conventional liquid culture methods the efficiency of a new technique for establishing lymphoid cell lines in which lymphoma cells were cultured initially in agar medium. Cell from 39/79 lymphomas gave rise to loose lymphoid colonies in the seeded agar after 7 days' incubation at 41 C. Two types of macrophage colony also developed. When lymphoid colonies in agar were transferred to liquid culture, 23/39 gave rise to permanent lymphoid cell lines, compared with 8/33 comparable cultures initiated in liquid medium. Twenty-nine new cell lines have been developed from Rhode Island Red, line 6 and line 7 chickens. All carry T-cell markers and the MD tumor-associated surface antigen (MATSA) and showed variable but low responsiveness to lectin mitogens. The new cell lines, when first established, consisted mainly of small, lymphocytoid cells but, after varying times, these changed into typical lymphoblastoid lines and an increased expression of an embryonic antigen was associated with this change. The lymphocytoid line cells were more slowly growing and density-dependent than were the lymphoblastoid cells, and lymphocytoid lines grew better at 41 C and lymphoblastoid lines better at 37 C. MD virus could be rescued from some of the lines but others appeared to be true nonproducers. (Author abstract) (21 Refs)

26. THE LACK OF ESTROGEN CONTROL OF RODENT ALPHA-FETOPROTEIN LEVELS.

Sheehan DM, Branham WS
Div. Teratogenesis Res., Natl. Center for Toxicological Res., Jefferson, AZ, 72079
Teratogenesis Carcinog Mutagen; 1(4):383-388 1981

The possible regulation of alphafetoprotein (AFP) by estrogens was investigated. Diluted plasma from adult mice fed diethylstilbestrol, estradiol, or control chow did not display any high affinity binding of estradiol, but did show nonsaturable low-affinity binding attributable to albumin. Plasma from 15-day-old rats bound estradiol with a KD = 0.5 x 10(-8) M. Daily injection of estradiol did not alter the plasma decay curve of AFP. Dissociation constants did not change with age or treatment with estrogens. The failure of estradiol to alter AFP levels was not due to a lack of biologically effective estrogen since the neonatal uterus showed a significant wt gain response under the same conditions. It was concluded that estradiol does not alter existing AFP levels in the neonatal rat. (39 Refs)

27. PERINATAL CHANGES OF ALPHA-FETOPROTEIN CONCENTRATION IN THE SERUM AND ITS SYNTHESIS IN THE LIVER OF ANALBUMINEMIC RATS.

Esumi H, Takahashi Y, Seki M, Sato S, Nagase S, Sugimura T
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Cancer Res; 42(1):306-308 1982

The profile of appearance and disappearance of alpha-fetoprotein (AFP) in the serum of analbuminemic rats, which have a genetically controlled lack of serum albumin, was studied. During the perinatal stage, AFP was present in the serum of analbuminemic rats, the concentration at birth being 10 mg/ml as in normal rats. In analbuminemic rats, the concentration of serum AFP remained at about 10 mg/ml during the 1st wk after birth and then decreased rapidly during the next 2 wk, becoming undetectable about 4 wk after birth. In normal rats, the serum AFP concentration reached a max of 11.5 mg/ml at birth and then decreased sharply to an undetectable level within 4 wk after birth, although a small rebound of AFP concentration was observed about 1 wk after birth. AFP synthesis in analbuminemic and normal rats was examined by injecting [3H]leucine ip and then measuring the radioactivity incorporated into the acid-insoluble fraction and immunoprecipitable fraction using anti-AFP antiserum. In analbuminemic rats, synthesis of AFP amounted to 7.5% of the total protein synthesis at birth and was maintained at about 7% of the total for the 1st wk after birth and then decreased to 2% at 2 wk after birth. In normal rats, AFP synthesis also amounted to 7.5% of the total protein synthesis at birth but decreased to about 2% at 2 days after birth and then remained at a low level for about 2 wk. In both normal and analbuminemic rats, AFP synthesis was undetectable at 4 wk after birth. These data show that AFP synthesis is shut off after birth irrespective of the serum albumin concentration during neonatal development. (Author abstract) (19 Refs)

IMMUNOLOGIC INTERACTIONS

28. PRODUCTION OF ANTIBODIES AGAINST ANTIGENS RELEASED FROM HUMAN PANCREATIC TUMOUR XENOGRAFTS.

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Dept. Surgery, St. George's Hosp. Medical Sch., London SW17 0RE, England
Br J Cancer; 44(3):388-395 1981

Antibodies directed against the antigens released from viable tumor cells during growth have been raised by cross-immunization of immunocompetent hairy litter-mates with serum from nude mice bearing pancreatic tumor xenografts. Antisera raised against the components released from a primary pancreatic tumor xenograft (WB) or from a tumor cell-line xenograft (GER) showed a titer greater than 1:625 against cultured pancreatic tumor cells by an I125-binding assay. Five out of 14 of the hairy litter-mates immunized with serum from the same tumor (GER) produced antisera that bound more strongly to pancreatic cancer cells than to 13 other non-pancreatic cell lines (binding ratio greater than 2). Absorption of the antisera with pure CEA reduced the level of binding by 11-25% without affecting the specificity for pancreatic tumor cells. The antibody response could be completely removed by absorption with pancreatic tumor cells, whereas 50% and 18% of the activity remained after absorption with normal pancreas homogenate and a mixed non-pancreatic tumor-cell pool, respectively. Immunofluorescent staining of pancreatic tumor sections indicated that the antibody was localized on the membrane of ductular epithelial cells. Challenge of immunocompetent mice using this procedure has produced a polyspecific antiserum with signs of selectivity for the circulating antigens released from pancreatic cancer cells, and may provide a route to the production of antibody against specific tumor components. (Author abstract) (31 Refs)

29. PURIFICATION OF SPECIFIC ANTIBODY TO ALPHA-FOETOPROTEIN AND ITS IMMUNOLOGICAL EFFECT ON CANCER CELLS.

Hirai H, Tsukada Y, Hara A, Hibi N, Nishi S, Wepsic HT, Koji T, Ishii N
Dept. Biochemistry, Hokkaido Univ. Sch. Med., Sapporo, Japan
J Chromatogr; 215:195-210 1981

Human or rat alpha-fetoprotein (AFP) was highly purified from ascitic fluid or serum of hepatoma bearers. The purification was carried out mainly by means of immunoadsorbent chromatography using Sepharose coupled to specific anti-AFP antibody with BrCN activation, and by Sephadex gel filtration. Horses were immunized with the purified AFP and the specific antibody was isolated from the antiserum by means of an immunoadsorbent coupled to purified AFP. The specific antibody was found to bind specifically with AFP-producing tumor cells. The antibody was applied for radio immunodetection of the tumor. 125I-labeled antibody was administered to patients or rats with hepatoma, and radioactivity localized in the tumors was scintiscanned with a scintillation camera. In this way, the location of the tumor was detected in about 50% of the hepatoma bearers. The cytotoxicity of the antibody was clearly demonstrated both in vitro and in vivo in animal experiments. The antibody was administered to patients with advanced hepatoma. Although no improvement of the disease was demonstrated, serum AFP levels decreased greatly and in some cases low AFP levels were maintained for long periods suggesting that the antibody suppressed AFP-producing hepatoma cells. No significant side effects were observed in patients who had been administered with the horse antibody. (Author abstract) (10 Refs)

30. A VINDESINE-ANTI-CEA CONJUGATE CYTOTOXIC FOR HUMAN CANCER CELLS IN VITRO.

Johnson JR, Ford CH, Newman CE, Woodhouse CS, Rowland GF, Simmonds RG
Surgical Immunology Unit, Clinical Oncology, Queen Elizabeth Hosp., Edgbaston, Birmingham B15 2TH, England
Br J Cancer; 44(3):472-475 1981

The ability of antibodies against carcinoembryonic antigen immunoglobulin (anti-CEA Ig) to enhance the cytotoxicity of vindesine was studied in the Calu-6 human lung cancer cell line. The anti-CEA conjugate produced a dose-dependent decrease in the fraction of surviving cells, while the conjugate of vindesine with normal sheep Ig had little effect on cell survival. The anti-CEA Ig alone had a low cytotoxicity. Simple mixing of vindesine and antibody did not amplify the drug effect. (15 Refs)

31. A NEW APPROACH TO THE IDENTIFICATION OF TUMOUR SPECIFIC ANTIBODIES IN PATIENTS WITH PANCREATIC CANCER (MEETING ABSTRACT).

Davies G, Grant AG, Duke D, Hermon-Taylor J
Department of Surgery, St. George's Hospital Medical School, London, England
Newsletter Natl Pancreas Cancer Project; VI(2):18 1981

Human pancreatic tumor xenografts grown in athymic nude mice have been shown to shed components into the serum of these animals which evoke a specific antibody response against pancreatic cancer cells when the tumor-bearing mouse serum is injected into immunocompetent hairy littermates. The availability of the athymic Rowett nude rat (RNU/RNU) which we have recently shown to be a suitable model for the growth of human gastrointestinal tumors from both primary explants and cancer cells in tissue culture enabled a serial study of this phenomenon. Twelve nude rats were implanted with 3 x 10(7) pancreatic cancer cells; 8 tumors grew progressively. Blood (1.7 ml) was taken from the tail vein of each animal before implantation and thereafter every 21 days for up to 9 mo. Unlike the nude mouse, antibodies against tumor cells were detected in the serum of tumor-bearing rats using a quantitative I125 membrane binding assay, but an antibody response was detectable whether the tumor grew or did not grow. Carcinoembryonic antigen (CEA) and alpha fetoprotein (AFP) were measured serially in animals in which tumors grew. There was less than 4 ng/ml AFP in the serum of 4 tumor-bearing animals after 7 mo growth with tumors measuring 12 cm2. A progressive rise in CEA up to 156 ng/ml during 9 mo of growth was only detected in 1 of these 4 animals. Immunization of 4 immunocompetent rat hairy littermates with serum from 8 animals bearing 12 cm2 tumors elicited an antibody response selective against pancreatic cancer cells when compared with a panel of 5 other human tumor cell lines (binding ratio greater than 1.7) and normal human lymphocytes (binding ratio 4.8). Such selectivity was not detected in serum from tumor bearing animals (binding ratio less than 1.1), suggesting that immunization of hairy littermates may offer a biological opportunity for specific antibody production against pancreatic cancer cells. (no Refs)

32. EFFECT OF LOCALIZED HYPERTHERMIA ON THE 'IN VIVO' AND 'IN VITRO' IMMUNE RESPONSE OF PATIENTS WITH ADVANCED CANCER (MEETING ABSTRACT).

Salama AM, Goutner A, Brule JM, Cosset JM, Dutreix J
Institute Gustave-Roussy, Villejuif, France
Strahlentherapie; 157(9):622 1981

Twenty-three patients with advanced cancer were subjected to localized hyperthermia by short-wave capacitive diathermy (27 MHz) for two wk in the order of 3 sessions a wk. Each session lasts one hr at the temperature of about 42 C. This group of patients was submitted for both cell and humoral immune tests, which are done on two occasions, two days before and after the hyperthermia course. Cell-mediated immune response was studied using both in vivo skin tests (delayed-type hypersensitivity DTH) to seven recall antigens. A 70% glycerin soln, the antigen diluent, is provided as a negative control; and in vitro tests which include response to mitogens and spontaneous cell-mediated cytotoxicity reaction. Humoral immunity was evaluated using immunoglobulin dosages (IgG, IgM, IgA) and that of complement fractions C'3 and C'4. In addition, full blood count, sedimentation rate and dosage of Carcino-embryonic Antigen (CEA) were estimated before and after hyperthermia course. The results of this study indicated that there is no significant modification of the dosages of immunoglobulins, CEA, C'3 and C'4 and equally that of sedimentation rate. DTH reactions were augmented in 14/23 patients. The responsiveness of lymphocytes for mitogens was diminished after hyperthermia in most cases. Lymphocytosis variations could not be correlated with the resposne to treatment. Effective tumor response to hyperthermia seemed to be associated with an increase in both natural killer reactivity and delayed type hypersensitivity reactions. (no Refs)

33. RADIOACTIVE ANTI-CEA ANTIBODIES IN CANCER THERAPY (MEETING ABSTRACT).

Goldenberg DM, Gaffar SA, Bennett SJ, Beach JL
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Oncodev Biol Med; AbstractsBook,1:27 1981

Radioactive antibodies to carcinoembryonic antigen (CEA) have been shown to be capable of locating CEA-neoplasms in animal systems and in humans by the method of radioimmunodetection. Experiments were undertaken to determine the antitumor effects of anti-CEA goat antibody labeled with I-131 in hamsters bearing the CEA-producing GW-39 human colonic carcinoma. At a single injection of 1 mCi I-131 and higher, a marked growth-inhibition of GW-39 tumors, as well as a considerable increase in survival time of the tumor-bearing hamsters, could be achieved. At a dosage of 1 mCi, the radioactive, affinity-purified antibody appeared to be superior to radioactive normal goat IgG in influencing tumor growth and survival time, but no significant difference could be seen at the higher dosage of 2 mCi given. Tumor/non-tumor ratios of specific antibody were 20-to 30-fold that of the normal IgG preparation. Radiobiological calculations indicated that the tumors received, at up to 20 days post therapy, 1,325 rads for the specific antibody, and only 411 rads for the normal IgG preparation. These findings support the use of antibodies to cancer markers for isotopic cancer therapy. (1 Ref)

34. USE AND LIMITATIONS OF 131I-LABELED MONOCLONAL ANTI-CEA ANTIBODIES FOR SCANNING DETECTION OF HUMAN CARCINOMAS (MEETING ABSTRACT).

Mach JP, Buchegger F, Forni M, Ritschard F, Accolla R, Carrel S
Ludwig Institute for Cancer Research, 1066 Epalinges, Lausanne, Switzerland
Oncodev Biol Med; AbstractsBook,1:29 1981

Monoclonal antibodies with a high specificity and affinity for carcinoembryonic antigens (CEA) were purified from hybridoma ascites, labeled with 131I and injected first in nude mice bearing human carcinoma grafts and later in tumor bearing patients. The results from the pilot human studies, obtained by external scanning of the patients and by direct measurement of the radioactivity in resected tumors and adjacent normal tissues, showed that monoclonal anti-CEA antibodies are capable of specific tumor localization in some patients. Ten out of 20 patients with colon or pancreas carcinoma injected with labeled monoclonal antibodies showed positive 'immuno-scintigraphy'. The specificity indices of localization obtained by comparing in fragments of tumor and normal tissues, the 131I radioactivity of the antibodies with the 125I radioactivity of control normal mouse IgG injected simultaneously with the antibodies, gave values ranging from 2-6. The non-specific accumulation of antibody radioactivity in the reticuloendothelium was much lower than with polyclonal antibodies. (2 Refs)

35. ROLE OF ONCOFETAL ANTIGEN IN REGULATION OF CELLULAR IMMUNITY DURING PREGNANCY AND TUMOR DEVELOPMENT (MEETING ABSTRACT).

Coggin JH
Department of Microbiology/Immunology, University of South Alabama, Mobile, AL, 36688
Oncodev Biol Med; AbstractsBook,1:38 1981

Tumor cells of the hamster and mouse induced by oncogenic DNA viruses carry cell surface antigens which are identical to those which appear temporally during fetal development in both species. We have established that immune regulation mediated by suppressor T lymphocytes (Ts) occurs during pregnancy and is directed against oncofetal antigen (OFA) determinants present on fetus and tumor cells. These Ts cells prevent cell mediated cytotoxic lymphocytes from killing fetal cells expressing OFA and similarly act against the killing of OFA positive tumor cells. A serum component, mediating non-specific suppression of Concanavalin A stimulation of hamster and mouse splenocytes can also be detected. The time course of the development of T suppressor cells which play an important role in immune regulation during pregnancy and a similar role during the development of OFA expressing tumor cells during early oncology are described. OFA can be released from fetal cell surfaces and has been characterized. (no Refs)

36. LOCALISATION OF MALIGNANT TERATOMA DEPOSITS BY EMISSION SCANNING AFTER INJECTION OF RADIO-LABELLED ANTIBODY TO ALPHA-FETOPROTEIN (MEETING ABSTRACT).

Fairweather DS, Bradwell AR, Dykes PW
Department of Immunology, University of Birmingham Medical School, Birmingham B15 2TJ, England
Clin Sci; 61(3):1P 1981

Alpha-fetoprotein (AFP) is used as a tumor marker in germ cell tumors. This study was performed to see if deposits of these tumors could be identified by external scanning after injection of radio-labelled antibody to AFP. The antibodies were raised in sheep by immunization with AFP extracted from amniotic fluid. After immunoadsorption with normal sera the IgG was further purified by ion-exchange chromatography. Samples were tested for acute toxicity and pyrogenicity in rabbits. The purified antibody was labelled with 131I using the Chloramine-T method and injected into the patients after an initial uneventful test dose. Before the scan, the patient also received 99mTc pertechnetate and 99mTc-labelled human serum albumin to outline the extra vascular space and blood pool to enable subtraction scanning to be performed. A total of 15 scans were performed on 12 patients, ten with Malignant Teratoma, one with an Endodermal Sinus Tumor and one with a Seminoma (used as a negative control). All nine patients with elevated serum AFP gave positive scans. Five of these were performed at the time of diagnosis and all abnormal areas were confirmed by computed tomographic (CT) scans and lymphangiography, although three secondary deposits were missed. Three patients gave normal scans when studied again after successful treatment, and when the serum AFP had fallen to normal. A further five gave positive scans, three of which were confirmed by CT scanning. These preliminary results show that it is possible to identify malignant teratoma deposits using antibody to AFP. (no Refs)

37. IDENTIFICATION OF ANTIGENIC DETERMINANTS INVOLVED IN CEA CROSS-REACTIVITY (MEETING ABSTRACT)

Laferte S, Krantz MJ
McGill Cancer Centre, Montreal, Canada
Oncodev Biol Med; AbstractsBook,1:P1 1981

We have purified from liver metastases of colon carcinoma a substance of mol wt 50,000 (50K), which by immunodiffusion is cross-reactive with carcinoembryonic antigen (CEA) and immunologically identical to an antigen found in a crude extract of normal spleen. This 50K antigen may therefore correspond to non-specific cross-reacting antigen. CEA and 50K have a similar amino acid composition. Fifty K has a lower overall carbohydrate content with relatively more mannose, and very little galactose and fucose. Partial proteolysis fragments of 50K were prepared using either trypsin, protease V8 or chymotrypsin. One immunoreactive fragment from each digestion mixture was purified by high pressure liquid chromatography (HPLC), giving products ranging between 20,000 and 30,000 mol wt. When the 3 HPLC peaks were tested in a radioimmunoassay for 50K, inhibitions reached a plateau at 50%, indicating that each fragment contained only half of the determinants found on the 50K molecule. When any two fragments were mixed, inhibition was not increased indicating that all 3 fragments contained the same subset of immunological determinants and suggesting that these fragments originate from the same part of the 50K molecule. To determine whether CEA-50K cross-reactivity resides in the available CEA and 50K fragments, we have carried out radioassays employing various fragments as radiolabel and the other fragments as inhibitors. The results showed that 50K fragments and CEA fragments compete for the same subset of anti-CEA antibodies. We conclude that these fragments contain determinants involved in CEA cross-reactivity. (no Refs)

38. MONOCLONAL ANTIBODIES TO CARCINOEMBRYONIC ANTIGEN (MEETING ABSTRACT)

Fuks A, Krantz MJ, Laferte S
McGill Cancer Center, Montreal, Canada
Oncodev Biol Med; AbstractsBook,1:P2 1981

Monoclonal antibodies to carcinoembryonic antigen (CEA) were developed by immunization of a Balb/c mouse with HCT-8R, a CEA-producing colonic adenocarcinoma cell line, and subsequent fusion of the immune splenocyte with P3-NS1/1-Ag4-1 mouse myeloma. Supernatants of hybrid cells were screened by a binding assay using purified radiolabeled CEA. Twenty-five of the 96 initial culture wells demonstrated anti-CEA reactivity and several of these have been cloned. The fine specificities of two of these antibodies were examined using radiolabeled CEA, the cross-reactive antigen 50,000 (50K), as well as proteolytic fragments derived from these molecules. The first antibody, b18.7.7, binds at high titre to CEA and to the major fragment derived from CEA by chemical cleavage at cysteine residues, as well as to the major fragment derived by trypsin, chymotrypsin or protease V8 digestion. Furthermore, this antibody reacts equally well with 50K, and its chymotryptic and protease V8 fragments. The second antibody d2.14.1, displays the same spectrum of reactivity as b18.7.7 with CEA and its fragments but its reactivity with 50K is significantly reduced compared with that of the first antibody. We conclude that the two anti-CEA monoclonal antibodies differ in their fine specificities towards the CEA molecule. (no Refs)

39. ALPHA-FETOPROTEIN ON HUMAN PERIPHERAL BLOOD LYMPHOCYTES DOES NOT BLOCK COMPLEMENT-DEPENDENT LYMPHOCYTOTOXICITY.

Ren EC, Chan SH
WHO Immunology Res. and Training Centre, Univ. Singapore, Singapore 0316, Singapore
Scand J Immunol; 14(3):309-313 1981

Using a direct immunofluorescence assay, we showed that alpha-fetoprotein (AFP) both in purified form and in hepatocellular carcinoma (HCC) sera was capable of binding onto 10-20% of T lymphocytes and 5-10% of B lymphocytes in human peripheral blood when these lymphocytes were preincubated in AFP-positive fluids at 4 C in the presence of sodium azide. But when the preincubation temperature was raised to 37 C, most of the membrane-bound AFP was internalized or shed, and, consequently, less than 3% of the cells showed positive membrane fluorescence. In addition, binding of AFP onto lymphocyte surface membrane and the continuous presence of large amounts of AFP in these lymphocyte cultures did not interfere with the action of cytotoxic antibodies directed against HLA determinants on the lymphocyte surface. (Author abstract) (15 Refs)

CLINICAL/ DIAGNOSIS/ IMMUNOTHERAPY

40. RECENT TRENDS IN TESTICULAR CANCER.

Anderson JD
Dept. Oncotherapy, Univ. Orange Free State, Bloemfontein, Orange Free State, South Africa
S Afr Cancer Bull; 25(1/2):51-57 1981

Diagnosis and treatment of testicular neoplasms (TN) are described. Hormone assays and immunological markers (beta chorionic gonadotropin, alpha-fetoprotein, and carcino-embryonic antigen) are starting to play an important role in the diagnosis of these neoplasms. Other techniques considered in relation to the evaluation of TN include lymphangiography, computed axial tomography, iv pyelograms, chest x-rays, and gallium scans. The proper management of TN depends on accurate staging. The two types of TN, seminomatous (STN) and non-seminomatous (NSTN) tumors, are described. STN are the most common type of TN tumor, being found in approx 2/3 of cases. The diagnosis and treatment of anaplastic, spermatocytic, and classic STN are considered. STN usually spread via lymphatics in an orderly fashion. STN are radiosensitive tumors, and cure can be expected following aggressive radiotherapy. Roles of surgery and chemotherapy in the treatment of STN are considered. NSTN occur in a younger age group than do STN. The mode of NSTN spread is orderly, but approx 60-70% of these tumors have retroperitoneal metastases at presentation. Management of NSTN has changed with the great efficacy of chemotherapy regimes presently being used. Survival rates now range from 75% to greater than 95% as compared with 40-60% 7 yr ago. Currently, NSTN treatment includes careful lymph node dissection and chemotherapy, with or without radiation. (17 Refs)

41. REPORT OF NINE CASES OF INTRACRANIAL CAVERNOMA.

Gi H, Mori K, Handa H
Dept. Neurosurgery, Kyoto Univ. Faculty Medicine, Kyoto, Japan
Neurol Surg; 9(3):267-276 1981

Nine cases (3 men, 6 women; 19-50 yr old) of intracranial cavernoma (CN) which were encountered during a 38-yr period were discussed. The CN were in the middle fossa in 4/9, cerebral hemisphere in 2/9, pons in 1/9, midbrain and scalp in 1/9, and third ventricle and hypothalamus in 1/9. Extra-axial masses with small flecked stains or tumor stains were detected with angiography in 3/4 cases of CN in the middle fossa; preoperatively these cases were diagnosed meningiomas. Use of radionuclide computed tomography in the case of CN of the occipital lobe indicated that delayed scans were useful for differential diagnosis of this tumor from meningioma. The case of CN of the hypothalamus and third ventricle was preoperatively misdiagnosed teratoma because of marked growth associated with elevation of carcinoembryonic antigen. Diagnosis and treatment of intracranial CN should focus on two findings: (1) CN occurring in the middle fossa differ from CN at other sites in that they hemorrhage easily during surgery, and (2) middle fossa CN occur often in middle-aged women, an important diagnostic difference between CN and meningiomas. (31 Refs) (In JPN)

42. LACTIC DEHYDROGENASE IN THE MONITORING AND PROGNOSIS OF TESTICULAR CANCER.

Lippert MC, Javadpour N
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Cancer; 48(10):2274-2278 1981

In a prospective study of 80 patients with germinal testicular cancer, serial determinations of lactic dehydrogenase (LDH), alpha-fetoprotein (AFP) and human chorionic gonadotrophin (HCG) were followed for a mean of 18.1 mo. Serum LDH was found to be elevated more frequently with increasing tumor bulk. LDH was elevated in 78.0% of the patients with Stage III disease but only 26.3% of the Stage II patients and 20.0% of the pre-orchiectomy Stage I patients. In this study, serum HCG and AFP levels were always elevated in the presence of elevated serum LDH levels except in one patient when LDH was the only elevated marker, in which case it correlated with clinical disease. Correlation of these three serum markers is shown by elevation of LDH in 78.0% of the Stage III patients, AFP in 78.6%, and HCG in 76.2%. In addition, of the 43 patients who had normal LDH levels on initial presentation, their mean survival time (MST) at the end of the study was 15.5 mo while the 26 patients who had elevated LDH levels on initial presentation had an MST of 9.2 mo. Serum LDH, therefore, may be useful in evaluating patient prognosis as well as an adjunct in monitoring the treatment of patients with bulky testicular cancer. The combination of LDH and HCG has been utilized to monitor the treatment of seminoma. (Author abstract) (16 Refs)

43. ONCOFOETAL ANTIGENS IN CANCER OF THE CERVIX AND OVARY.

Cauchi MN, Koh SH, Lim D, Hay DL
Dept. Pathology, Royal Women's Hosp., Melbourne, Victoria, Australia
Br J Cancer; 44(3):403-409 1981

The incidence of oncofetal antigens has been reported to be increased in patients with gynecological cancers. In this study the incidence of CEA, AFP, and hCG (beta subunit) were studied in patients with adenocarcinoma of the ovary, adenocarcinoma of the cervix, and squamous-cell carcinoma of the cervix. Using a low cut-off point (CEA 2.5 ug/liter, AFP 5 ug/liter, and hCG 3 iu/liter) there is an unaccep tably high proportion of control patients having one or more positive tests (42-54%) compared to cancer-bearing patients (67%). The specificity of the tests can be increased to over 95% by increasing the cut-off point to CEA 10 ug/liter, AFP 10 ug/liter, and hCG 10 i.u./liter. Although this reduces the sensitivity considerably, the incidence of false positive in the control population is reduced to nil in non-cancer patients and to 2% in cancer patients tested when free of tumor, compared to 17% of patients with cancer of the ovary, 33% with adenocarcinoma of the cervix, and 6% with squamous-cell carcinoma of the cervix. Patients with adenocarcinoma of the cervix were clearly distinguishable from those with squamous-cell carcinoma of the cervix by these tests. There was also a significant correlation between AFP and hCG levels in adenocarcinoma of the cervix ($r = 0.53$, p less than 0.05). (Author abstract) (19 Refs)

44. COMBINED EFFUSION FLUID TUMOR MARKER ASSAY, CARCINOEMBRYONIC ANTIGEN (CEA) AND HUMAN CHORIONIC GONADOTROPIN (HCG), IN THE DETECTION OF MALIGNANT TUMORS.

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Dept. Pathology, St. Joseph's Hosp., 350 North Wilmot Road, Tucson, AZ, 85711
Cancer; 48(11):2475-2479 1981

Carcinoembryonic antigen (CEA) and human chorionic gonadotropin (hCG) and protein concentrations were determined on 81 random pleural and ascitic effusions submitted for cytologic examination. CEA and hCG assay results were expressed as direct concentrations and with respect to total protein concentration. Levels of significance for malignant fluids were established as follows: CEA greater than or equal to 10 ng/ml, hCG greater than or equal to 10 mIU/ml, CEA greater than or equal to 500 ng/g protein, hCG greater than or equal to 500 mIU/g protein. Clinical follow-up demonstrated 55 fluids associated with coexisting malignant tumors and 26 fluids not associated with malignancies. This study suggests effusion fluid CEA and hCG assay may provide a useful adjunct to cytology in the evaluation of effusion fluids for malignancy. Assay results, furthermore, may be more accurately expressed with respect to effusion protein concentration. (Author abstract) (11 Refs)

45. AFP IN YOLK SAC TUMOR AND SOLID TERATOMA OF THE OVARY: SIGNIFICANCE OF POSTOPERATIVE SERUM AFP.

Ishiguro T, Yoshida Y, Tenzaki T, Ohshima M, Suzuki H
Dept. Obstetrics and Gynecology, Shiga Univ. Medical Science, Seta, Ohtsu 520-21, Japan
Cancer; 48(11):2480-2484 1981

Serial serum alpha-fetoprotein (AFP) was examined postoperatively in five patients with yolk sac tumor and in three with solid teratoma of the ovary. Serial estimation of AFP was also done in sera from postpartum patients to compare the decreasing ratio between the two groups. Serum AFP in these postpartum women decreased according to the exponential function curve as $AFP = be^{-mx}$ (x = days a fter delivery) with a mean m value of 0.1652 and a mean correlation coefficient of 0.9911. Half-time of serum AFP in postpartum subjects was 4.33 days. Exponential decrease of serum AFP was also found in postoperative patients with yolk sac tumor and solid teratoma of the ovary. However, in those in whom there was an incomplete removal of the tumors, the values of either m or coefficient of correlation were significantly lower as compared to those in patients with complete extirpation of lesions or those in postpartum subjects. Elevation of serum AFP was noted postoperatively in two patients with recurrences; however, significant decreases in AFP following chemotherapy were apparent in one patient with immature solid teratoma. These findings suggest that the decreasing ratio of postoperative serum AFP is an effective indicator to determine whether or not the lesions were completely extirpated, although a normal value may not always imply the absence of microscopic metastasis of tumor cells. Serial estimation of serum AFP was of value in assessing the presence of recurrences and evaluating the efficacy of chemotherapy. (Author abstract) (12 Refs)

46. CARCINOEMBRYONIC ANTIGEN (CEA) IN THE CLINICAL DIAGNOSIS AND TREATMENT OF COLORECTAL CANCER.

International Cancer Research Data Bank
NCI, Westwood Building, Room 10A18, Bethesda, MD, 20205
Carcinoembryonic Antigen (CEA) in the Clinical Diagnosis and Treatment of Colorectal Cancer (Oncology Overview) Bedikian, A Y, ed This Title is Available through National Technical Information Service, Springfield, VA, as NTISUB/PB81-922808:; OT-81/08:106pp. 1981

ONCOLOGY OVERVIEW is a service of the International Cancer Research Data Bank (ICRDB) Program of the National Cancer Institute. Retrospective bibliographies containing 100-500 selected abstracts of published research on topics of high interest to cancer investigators are presented. The scope of this OVERVIEW covers carcinoembryonic antigen (CEA) in the clinical diagnosis and treatment of colorectal cancer. Areas covered include the presence of CEA in plasma, colonic lavage, feces, secretions and tissue of different patient populations, the heterogeneity of human CEA molecules, the role of CEA in diagnosis and screening, the use of CEA in the surgical management of colorectal cancer as a malignancy following resection, the utility of CEA in monitoring responses of colorectal cancer to chemotherapy, chemoimmunotherapy, and radiation therapy. Also included are preclinical studies involving the synthesis of CEA and the effect of therapy on CEA production in experimental human colorectal tumors. Studies on the use of labeled CEA antibodies for radioimmunodetection of malignancy in animals and humans are also covered in this OVERVIEW.

47. EVALUATION OF VARIOUS METHODS OF DIAGNOSING MALIGNANT TUMORS OF THE SMALL INTEST INE.

Asakura H, Watanabe M, Aiso S, Miura S, Kobayashi K, Hibi T, Morishita T, Tsuchiya M, Sugino Y, Kumakura K
Dept. Internal Medicine, Keio Univ. Sch. Medicine, Tokyo, Japan
I To Cho; 16(9):999-1006 1981

Various methods of diagnosis (clinical symptoms, common clinical laboratory tests, gastrointestinal roentgenography, abdominal angiography, small intestinal enteroscopy, and computed tomography scan) were evaluated in 10 cases (6 men, 4 women; 49-64 yr old) of malignant tumors of the small intestine. The tumors were carcinoma (3), leiomyosarcoma (4), and malignant lymphoma (3). There were no distinctive clinical symptoms; bowel obstruction was observed in three, abdominal pain in eight, bloody stools in one, and abdominal swelling in three. Mild iron-deficiency anemia and occult blood were observed in all patients, and one patient had high levels of serum carcinoembryonic antigen. Double-contrast roentgenography performed with intubation was excellent for diagnosing presence and location of tumors, and although each tumor type had characteristic x-ray patterns, similarity of x-ray findings in some cases made differential diagnosis difficult. Enteroscopy for macroscopic observation and biopsy for microscopic observation were the best means of diagnosis, but procedural problems existed for each of these methods. Angiography was thought to be more useful in diagnosis of small intestinal tumors than tumors of other organs; angiography was particularly useful with leiomyosarcoma but not very useful with carcinoma. Computed tomographic scans were useful in visualizing intestinal thickening and tumor patterns outside and inside the intestinal canal. (31 Refs) (In JPN)

48. STUDIES OF GASTRIC JUICE OF GASTRIC CANCER PATIENTS FROM THE IMMUNOLOGICAL POINT OF VIEW.

Ishigami H, Fujimoto S, Minami T, Akao T, Kitsukawa Y, Takahashi M, Miyazaki M, Okui K
First Dept. Surgery, Chiba Univ., Sch. Medicine, Inohana, Chiba 280, Japan
Rinsho Meneki; 13(Suppl2):124-132 1981

In order to determine the root of the previously reported immunosuppressive activity of gastric juice from gastric cancer patients, carcinoembryonic antigen (CEA), alpha-fetoprotein, and alpha2-macroglobulin, in gastric juice extracts were measured. Fresh gastric juice was collected from 7 healthy volunteers, 4 peptic ulcer patients and 21 gastric cancer patients, under tetragastric stimulation, and adjusted to pH 7. They were centrifuged at 2,000xg and the supernatants were lyophilized. These gastric juice extracts, which were dissolved in 0.9% NaCl soln, were assayed for protein concentration by Lowry's method and adjusted to a protein concentration of 100 ug/ml. The mean CEA level of gastric cancer juice extracts was higher than that of healthy volunteers or peptic ulcer patients. No relationship between CEA leve ls of serum and gastric juice existed in 17 gastric cancer patients. An inverse relationship between tumor size and gastric juice CEA level was observed in 19 patients with resectable gastric cancer. Of the 32 gastric juice extracts, 3, all from gastric cancer patients, had alpha-fetoprotein levels above 5 ng/100 ug of protein. No special relationship was found between serum and gastric juice alpha-fetoprotein levels in gastric cancer patients. Five gastric juice extracts (4 from gastric cancer patients) had more than 12 ug of alpha2-macroglobulin per 100 ug of protein. It is speculated that oncofetal antigens are partially concerned with the immunosuppression of gastric juice extracts from gastric cancer patients. (21 Refs) (In JPN)

49. THE SERUM LEVELS OF HUMAN ALPHA-FETOPROTEIN, AFP, CHORIOGONADOTROPIN, HCG, PLACENTAL LACTOGEN, HPL, AND PREGNANCY-SPECIFIC BETA1-GLYCOPROTEIN, SP1, ARE OF NO CLINICAL SIGNIFICANCE IN COLORECTAL CARCINOMA.

Szymendera JJ, Kaminska JA, Nowacki MP, Szawlowski AW, Gadek A
Dept. Nuclear Medicine, Inst. Oncology, Post Office Box 47, PL-00973 Warsaw 22, Poland
Eur J Cancer Clin Oncol; 17(9):1047-1052 1981

Four biochemical tumor markers were measured by radioimmunoassays in sera of 233 patients with colorectal carcinoma. Pre-operative serum levels of AFP, hCG, hPL and SP1 were elevated in 1.3, 5.4, 4.8 and 0.7% of the patients respectively.

Post-operative serum levels either increased transiently or were elevated permanently. Even when an elevation of one or more of the markers was fairly stable, it rarely provided useful information, since sensitivity of the test, ie ratio of true positives to all patients with recurrence, ranged from 0% for AFP to 15% for hCG. The predictive value of an elevated level of any marker for the diagnosis of recurrence was either misleading or equivocal, which makes each of no value for decision strategy for the individual patient. Therefore, determination in serum of any of these markers in patients with colorectal carcinoma does not seem to provide useful information for pre-operative diagnosis, nor for post-operative monitoring aimed at the detection of operable recurrence. (Author abstract) (33 Refs)

50. COMPUTERIZED TOMOGRAPHY IN ASSAYING EFFECT OF THERAPY IN PANCREATIC CANCER, PRELIMINARY RESULTS (MEETING ABSTRACT).

Kalser MH, Hill M, Redlhammer D, Barkin JS, Raskin J, Lessner H
University of Miami/Jackson Memorial Medical Center, Miami, FL
Newsletter Natl Pancreas Cancer Project; VI(2):30 1981

Serial computerized tomography (CT) scans were obtained before and after therapy in 58 patients with histologically proven pancreatic adenocarcinoma of the exocrine pancreas. Patients were grouped as to stage of disease prior to therapy. Four had resectable lesions (Group I), 31 had local extension and were not resectable but did not have distant metastases (Group II), and 23 had distant metastases (Group III). Of the patients in Group I, two are alive (mean survival of 60 mo), one died of distant metastases and one of vascular disease. None of the four had evidence of local recurrence. Group II patients were treated with radiation and chemotherapy. Six showed a significant decrease while 17 showed a significant increase in the area of the original tumor. The cause of death in both those with a decrease or increase in the size of the index lesion was distant metastasis. Group III patients, despite treatment with chemotherapy, showed a significant increase in the size of the tumor mass. Serum carcinoembryonic antigen (CEA) revealed no change in Group II patients whose lesions decreased in size, whereas there was a significant increase in those whose index lesions significantly increased in size. A significant increase of CEA occurred in patients of Group III. In conclusion, these preliminary observations demonstrate that CT scanning is of value in following the efficacy of therapy of the primary lesion in pancreatic adenocarcinoma. (no Refs)

51. THE USE OF CEA IN THE JAUNDICED PATIENT: DIAGNOSIS, STAGING, FOLLOW-UP, PROGNOSIS (MEETING ABSTRACT).

Martin EW, Strah K, Ferrara J, Martin DT, Cooperman M
The Department of Surgery, The Ohio State University College of Medicine, Columbus, OH, 43210
Newsletter Natl Pancreas Cancer Project; VI(2):39 1981

Preoperative plasma carcinoembryonic antigen (CEA) levels were determined by Roche Assay in 100 jaundiced patients, 78 with malignant disease and 22 with benign disease. Levels were above 4.0 ng/ml in 50 of 54 (92.6%) with pancreatic cancer, 15 of 18 (83.3%) with cholangiocarcinoma, 3 of 4 (75%) with ampullary cancer, and 1 of 2 (50%) with gallbladder cancer. Only 4 of 22 patients (18%) with benign disease had levels above 4.0 ng/ml. A preoperative CEA above 10.0 ng/ml was even more significant; no patient with benign disease had values over 7.5 ng/ml. On the contrary, 30 of 78 patients with proved malignant disease who had CEA levels above 10 ng/ml had unresectable tumors, and only 3 are living. Preoperative CEA values are helpful to the surgeon as an indication of resectability of tumor and to all clinicians in arriving at a realistic prognosis. Serial CEA determinations have proved useful in following the progression of the disease and in evaluating treatment. (no Refs)

52. DAUNOMYCIN TARGETING TO HUMAN COLON CARCINOMA CELLS USING MONOCLONAL ANTIBODIES (MEETING ABSTRACT).

Page M, Emond JP, Gauthier C, Dufour C
Department of Biochemistry, Universite Laval, Laval, Quebec, Canada
Oncodev Biol Med; AbstractsBook,1:24 1981

A new approach to chemotherapy using monoclonal antibodies for drug targeting to the tumor cell is reported. Daunomycin was covalently bound to monoclonal antibodies directed against carcinoembryonic antigen (CEA) with 0.01% glutaraldehyde in various drug:protein ratios. The pharmacological activity of the drug-antibody conjugate was assayed in vitro with human colon adenocarcinoma cells producing CEA. Using a drug:protein ratio of 5.7, the inhibition of thymidine incorporation was measured at various concentrations. At 500 ng/ml, the activity of antibody bound daunomycin was 800% the activity of an equivalent amount of free daunomycin; the activity of free antibody was only 2.2% while the physical addition of both antibody and daunomycin gave 116% of the activity of the free drug alone. A 60 min incubation period of the conjugate with adenocarcinoma cells was sufficient to obtain this effect. This new approach offers a potential application in cancer treatment since the drug carrier is directed against an already used cancer marker. (no Refs)

53. APPLICABILITY OF SINGLE AND SIMULTANEOUS MARKER MEASUREMENT (CEA, TPA, TAG) FOR DIAGNOSIS AND MONITORING IN PATIENTS WITH CANCER OF THE GASTROINTESTINAL TRACT (MEETING ABSTRACT).

Oehr P, Bormann R, Biersack HJ, Winkler C
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Oncodev Biol Med; AbstractsBook,1:29 1981

We investigated whether single or simultaneous use of one, two or three different antigens could enhance the sensitivity in diagnosis and its applicability for monitoring. We used carcinoembryonic antigen-enzyme immunoassay (CEA-EIA), tumor-derived polypeptide antigen-radioimmunoassay (TPA-RIA) and TennaGen (TAG)-HAI. Samples of more than 100 individual patients were determined. In order to compare the markers a normal value distribution of blood donors was established and the normal value fixed by setting 7.5% false positives for each antigen. CEA gave a sensitivity of 57%, TPA 63%, TAG 58%. Simultaneous measurement showed for CEA/TAG 76.3%, CEA/TPA 77.3%, TAG/TPA 82.5%. All markers combined showed 89% sensitivity. Each antigen appeared to be independent from each other as determined by correlation analysis and clinical follow up concerning treatment. (no Refs)

54. INCIDENCE AND MOLECULAR VARIANTS OF SP-1 IN PATIENTS WITH TESTICULAR GERM CELL TUMOURS (MEETING ABSTRACT).

Lamerz R, Mann K, Eiermann W, Lohrs U, Nathrath W
Department of Medicine II, Medical Centre Grosshadern, University of Munich, Munich, W. Germany
Oncodev Biol Med; AbstractsBook,1:56 1981

SP-1 was determined by commercial radioimmunoassay and enzyme immunoassay in sera of 42 patients with seminoma and 151 patients with non-seminomatous germ cell testicular tumors (NSGCT). The incidence rate was compared to that of alpha fetoprotein (AFP) and human chorionic gonadotropin (hCG) measured by radioimmunoassays developed by our laboratory. None of seminoma patients showed elevated SP-1 levels in contrast to 14/151 (9.3%) patients with NSGCT covering a range of 10 to 896 ng/ml. In comparison to the other 2 established markers, SP-1 elevations were never found in AFP-and hCG-negative nor AFP-positive/hCG-negative cases, but in 2.6% of AFP-negative/hCG-positive and in 6.6% of AFP- and hCG-positive cases. By indirect immunoperoxidase staining technique, SP-1 could be demonstrated in syncytiotrophoblastic giant cells of 11 cases investigated. During follow-up of 9 patients, SP-1 levels were low in comparison to hCG levels, reached their normal range sooner following therapy, and hence were less indicative of tumor disappearance. Gel filtration studies in single cases revealed the existence of a high mol wt variant in addition to the main SP-1 component which coeluted with purified 125-I-SP-1. By the results it is concluded that SP-1 determinations in patients with testicular germ cell tumors give no further significant information to the established tumor markers AFP and hCG. (no Refs)

55. PREOPERATIVE SERUM CEA CONCENTRATION AND CLINICAL STAGING AS PROGNOSTIC FACTORS IN COLORECTAL CANCER (MEETING ABSTRACT).

Staab HJ, Brummendorf T, Anderer FA
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Oncodev Biol Med; AbstractsBook,1:61 1981

Most of the earlier investigations on the prognostic value of the preoperative serum carcinoembryonic antigen (CEA) concentration in cancer patients examined its correlation with disease recurrence. In this report observed survival time was computed for 563 patients registered for resection of colorectal cancer since 1974. Significant difference in the survival rate was found for patients with different resectability, with different tumor extension and with different ranges of preoperative serum CEA concentrations. In addition, preoperative CEA concentration represented a significant gain in prognostic information within groups of patients with distinct resectability or/and tumor extension. The results indicated strongly that the preoperative serum CEA concentration seems to be an independent prognostic criterion within a group of clinically defined patients with comparable resectability and identical tumor, node, metastasis classification of their tumors. Therefore preoperative CEA determination, which can be established within about 10 days during hospitalization for primary treatment, should be included in clinical methods to give further information on patients with high risk. (no Refs)

56. USEFULNESS OF SERUM ALPHA-FETOPROTEIN IN THE DIAGNOSIS OF MINUTE HEPATOCELLULAR CARCINOMA (MEETING ABSTRACT).

Kusumoto Y, Munehisa T, Nakata K, Muro T, Kono K, Furukawa R, Ishii N, Koji T, Nagataki S
First Department of Internal Medicine, Nagasaki University School of Medicine, Nagasaki, Japan
Oncodev Biol Med; AbstractsBook,1:P65 1981

There is disagreement in the literature concerning the usefulness of the determination of serum alpha-fetoprotein (AFP) concentration in detecting minute hepatocellular carcinoma (HCC). The present study was undertaken, therefore, to investigate changes in serum AFP concentrations retrospectively in 15 patients with minute HCC (less than 5 cm in diameter). Eleven of them were operated to remove HCC and the diagnosis was confirmed by histology. Six of them were still alive and a patient received the second partial hepatectomy because of newly developed minute HCC 7 yr after the first operation. In 11 patients (80%) among these 15 patients with minute HCC, the diagnosis was initially suspected from the elevation of serum AFP concentrations when they had no clinical signs of HCC. Three patients showed the increased serum AFP concentrations at their first visits. However, in the other 8 patients, sudden elevation of serum AFP levels was detected during the follow up of cirrhotic patients whose serum AFP concentrations were measured once every one or two mo. The final diagnosis before operation was obtained by the hepatic angiography, computed tomography, ultrasonic echography and/or laparoscopic examination. The results suggest that the determination of serum AFP concentration is useful in suspecting minute HCC especially when serum AFP levels are determined regularly during the follow-up of cirrhotic patients. (no Refs)

57. CHEMOTHERAPY OF NON-SEMINOMATOUS TESTIS TUMOURS-ITS VALUE AND ITS PROBLEMS (MEETING ABSTRACT).

Colls BM
Christchurch Hospital, Christchurch, New Zealand
Br J Urol; 53(1):68 1981

Disseminated malignant teratoma of the testis has always offered clinicians a severe therapeutic challenge. Surgery and radiotherapy can hope to cure only early disease. The development of effective chemotherapy in association with retroperitoneal node dissection has revolutionized the outlook and promises to displace radiotherapy. Monitoring of serum alpha-fetoprotein and beta-subunit human chorionic gonadotropin tumor markers, which are found in some 80% of cases, has also assisted. Twenty yr ago the results of chemotherapy produced 7% long-term survivors; now, using the regime described by Einhorn and Donohue (1977), 74% of patients with disseminated tumors had a complete remission. In addition, survivors of this regime may be cured, since most relapses occur within 2 yr of treatment. Combined cyclical chemotherapy regimes are not without their problems; they are labor-intensive and produce adverse effects which, unless handled skillfully, are unacceptable. The Einhorn agents are: cis-platinum, which causes considerable nausea and vomiting, alopecia, renal damage and ototoxicity; bleomycin, which causes fever, rigors and interstitial pulmonary damage; vinblastine, which is a potent marrow toxin. The Christchurch experience with the Einhorn regime includes 18 evaluable cases. In all 18 cases an objective improvement was obtained and 13 entered complete remission. Adverse reactions were frequent, but acceptable. (1 Ref)

58. CEA, AFP, FSH, LH, HCG-B AND PRL VALUES IN THE SERUM OF UTERINE CERVICAL CANCER PATIENTS (MEETING ABSTRACT).

Hsu CT, Hsu TH, Chen WH
Department of Obstetrics and Gynaecology, Taipei Medical College, Taipei, China
Obstetrics and Gynaecology: 8th Asian Congress, October 25-31, 1981, Melbourne, Australia. Asia and Oceania Federation of Obstetricians and Gynaecologists 352 pp., 1981.

One hundred and four out of 224 (46.43%) uterine cervical cancer patients showed elevated carcinoembryonic antigen (CEA), 31 out of 222 (13.96% patients elevated luteinizing hormone (LH), 23 out of 220 (10.45%) patients elevated follicle stimulating hormone (FSH), 78 out of 216 (36.11%) patients elevated prolactin, 6 out of 216 (2.78%) patients elevated alpha-fetoprotein (AFP) and 15 out of 224 (6.70%) patients elevated human chorionic gonadotropin (hCG-b). Only CEA showed a correlation with the size of the primary tumor, and stage of the disease, and also possessed a clinical significance in detection of recurrence. High hCG-b values seems to be somewhat related to poor prognosis. A high PRL value also is of some clinical significance, however, not definite. AFP, FSH and LH seem less significant in prognostication. These findings will be illustrated with some particular cases. (no Refs)

59. CLINICAL SIGNIFICANCE OF MEASUREMENTS OF CARCINOEMBRYONIC ANTIGEN IN SERUM OF PATIENTS WITH CARCINOMA OF THE UTERINE CERVIX.

Braun P, Hildenbrand G, Izbicki J, Leyendecker G
Dept. Obstetrics and Gynecology, Univ. Bonn, D-5300 Bonn-Venusberg, W. Germany
Arch Gynecol; 230(4):263-273 1981

Serum carcinoembryonic antigen (CEA) levels were measured in 108 patients suffering from carcinoma of the uterine cervix before and immediately after treatment. Follow-up was extended for up to 990 days. In 88 of these patients (age 33-80 yr), the CEA levels were determined serially beginning with detection of the disease. In 20 patients (age 40-80 yr) the study was begun when diagnosis of recurrent disease was made. Three patients with stage Ib disease were treated by radical hysterectomy and pelvic lymphadenectomy. The remaining patients were treated with combined radiation therapy consisting of local application of radium 2-3x with a total dose of up to 5,200 mgeh and external radiation. A total dose of 40 Gy2 was given to the parametrium through two anterior and posterior portals. The highest value of CEA measured in a control group of healthy subjects was 12 nanog/ml. Of 88 patients with cervical carcinoma, 38 had values greater than 12 nanog/ml. Positive correlation could be made between elevated CEA and clinical stage of disease. CEA level before treatment was not prognostic for survival, but level after therapy indicated median survival time. (19 Refs)

60. CARCINOEMBRYONIC ANTIGEN: A USEFUL MONITOR OF THERAPY OF SMALL CELL LUNG CANCER.

Goslin RH, Skarin AT, Zamcheck N
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JAMA; 246(19):2173-2176 1981

In 85 patients with small cell cancer of the lung, the degree of carcinoembryonic antigen (CEA) elevation correlated with the extent of disease. Normal CEA levels (less than 2.5 ng/mL) occurred in 55% of patients with limited disease compared with 12% of patients with extensive disease. All patients with CEA levels greater than 50 ng/mL had liver involvement. Serial CEA levels were useful in monitoring response to chemotherapy and in predicting relapse. All patients with CEA values greater than 5.0 ng/mL before start of treatment had a fall in CEA level with response to treatment and a rise in CEA level when resistance to chemotherapy developed. In patients with CEA levels of less than 5.0 ng/mL at the start of treatment, rising values reflected the onset of recurrent disease in 10 of 21 patients who had relapses. The CEA levels used in conjunction with standard roentgenograms and organ scanning studies can aid in the initial staging of small cell cancer of the lung, and in monitoring treatment. (Author abstract) (26 Refs)

61. ALTERED DYNAMICS OF ALPHA-FETOPROTEIN PRODUCTION FOLLOWING PYRIDOXINE AND ADENOSINE 5'-TRIPHOSPHATE ADMINISTRATION TO CIRRHOTIC PATIENTS WITH OR WITHOUT PRIMARY HEPATOMAS AND TO LIVER-INJURED AND HEPATOMA-BEARING RATS.

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Oncodev Biol Med; 2(5):313-321 1981

Serum alpha-fetoprotein (AFP) levels were determined in 100 patients with liver cirrhosis. Of the 50 patients with cirrhosis and primary hepatomas, 35 had AFP levels higher than 10(4) (ng)/ml. Serum AFP levels remained low (less than 200 ng/ml) in 8/50 patients with hepatomas, and in 5/50 in this group the levels were between 200 and 2,000 ng/ml. The highest AFP level found in patients with cirrhosis alone was 1,600 ng/ml. In 12 patients with chronic liver disease without clinical evidence of hepatoma and whom subsequently developed primary hepatomas over a 2 to 32 yr follow-up period, AFP levels were not useful for earlier detection. In rats with livers injured by CCl4, simultaneous injections of pyridoxine and adenosine 5'-triphosphate (ATP) resulted in significant decreases of elevated serum AFP levels. However, this treatment had no effect on the AFP levels in 3'-methyl-4-dimethylaminoazobenzene induced hepatoma-bearing rats. Ten men with cirrhosis followed for 0.4 to 24 yr were treated with pyridoxine-ATP infusion for approx 12 to 30 days. In patients with no evidence of hepatoma, increased serum AFP levels diminished gradually following treatment. In patients with definite hepatoma the serum AFP levels increased. None of the hepatoma patients responded to the treatment. These results may offer a new approach to the earlier detection of primary hepatomas in these patients. (15 Refs)

62. LOCALIZATION OF EARLY RECURRENCE OF CARCINOMA OF THE COLON OR RECTUM BY RADIOIMMUNODETECTION IN PATIENTS WITH A RISING SERUM CARCINOEMBRYONIC ANTIGEN CONCENTRATION (MEETING ABSTRACT).

Begent RH, Keep PA, Searle F, Dent J, Bagshawe KD, Jones BE, Jewkes RF, Vernon P
Department of Medical Oncology, Charing Cross Hospital, London, W6 8RF, England
Oncodev Biol Med; AbstractsBook,1:P62 1981

Radioimmunodetection (RID) for localization of carcinoma of the colon or rectum by external scintigraphy after injection of 131 Iodine labelled antibody to carcinoembryonic antigen (CEA) has been reported. The purpose of this study was to investigate whether the method could be used to localize recurrence of carcinoma of the colon and rectum which have been predicted by rises in concentration of serum CEA during follow-up after apparently curative resection. RID was performed using the method of Goldenberg in 10 patients with raised serum CEA in the absence of symptoms or physical signs of recurrence. RID was positive in 9, the sites being liver alone, 3; liver and para-aortic nodes, 1; liver and retrovesical area, 1; liver and colon, 1; perineum, 1; bone, 1; para-colic area, 1. These recurrences have been confirmed unequivocally in 4 patients. While recurrence is likely in the remaining 5 patients it has not been definitely demonstrated by conventional radiology or surgery. These preliminary data suggest that RID may be useful in the investigation of patients in whom subclinical recurrence of carcinoma of the colon or rectum is suspected. In its present form it can be used to indicate which sites of suspected recurrence should be further investigated. (1 Ref)

63. PLASMA ALPHA-1 ACID GLYCOPROTEIN: A PROGNOSTIC INDICATOR IN METASTATIC AND UNRESECTABLE GASTRIC CARCINOMA (MEETING ABSTRACT).

Chu CY, Rashid S, Lai LT
Department of Medicine, Wayne State University, Detroit, MI
Oncodev Biol Med; AbstractsBook,1:P63 1981

Postoperative plasma alpha-1-acid glycoprotein (AAG) and carcinoembryonic antigen (CEA) levels in 9 patients with unresectable gastric carcinoma and 14 patients with metastatic gastric carcinoma after initial gastric resection were tested for the correlation with the extent of the disease as well as the survival time. CEA was assayed by Hoffmann LaRoche method with an upper limit of 12.5 ng/ml. Blood samples taken at the time of the first follow up date for unresectable cases and at the time of metastasis discovered for initially resectable cases. Two survival curves were constructed according to plasma AAG levels: 1 with AAG greater than 1.34 (25% above the upper limit) and the other less than 1.34 mg/ml. Wilcoxon rank sum test was used to compare these 2 curves. A significant difference among these 2 curves was found. Survival curves constructed according to plasma CEA levels greater than 15.6 ng/ml (25% above the normal upper limit) and less than 15.6 ng/ml showed no statistical difference. Seventeen patients received chemotherapy and 14 had repeated AAG assay and 12 had repeated CEA assay. The correlation between the changes of plasma AAG and CEA levels and the survival time from the date that chemotherapy started to the date of death were examined by the Spearman rank correlation test. It was found that the change of AAG but not CEA levels correlated with the survival time. (no Refs)

64. THE CLINICAL USEFULNESS OF PANCREATIC ONCOFETAL ANTIGEN IN SERUM FOR SCREENING THE PANCREATIC CANCER (MEETING ABSTRACT).

Oguchi H, Homma T, Kawa S, Nagata A, Furuta S
Department of Internal Medicine, Shinshu University School of Medicine, 3-1-1 Asahi, Matsumoto, Japan
Oncodev Biol Med; AbstractsBook,1:P64 1981

We have studied the characterization of pancreatic oncofetal antigen (POA) and its clinical application for the diagnosis of pancreatic cancer since 1972. In this paper, we investigated the usefulness of this POA for screening the pancreatic cancer. Four hundred and forty out-patients with abdominal complaints were tested for POA and also for carcinoembryonic antigen (CEA). Ouchterlony gel diffusion method was applied for POA assay and radioimmunoassay for CEA. Among the 440 patients, POA was positive in 13 cases. There were 3 cases with pancreatic cancer, 4 with malignancy of various organs and 6 with non-malignancy. Thirty-three of these 440 patients were found to have a malignancy in various organs. Of these 33, 7 were positive POA, 12 for CEA and 17 either for POA or CEA. As to the 5 cases with pancreatic cancer diagnosed by angiography and ERCP in this study, 3 were positive for POA, 2 for CEA and 4 either for POA or CEA. These results indicate that the measurement of POA is useful in screening the pancreatic cancer and the detection rate of pancreatic cancer becomes higher when POA and CEA were assayed simultaneously. (no Refs)

65. CEA AS A CANCER MARKER.

Goldenberg DM, Neville AM, Carter AC, Go VL, Holyoke ED, Isselbacher KJ, Schein PS, Schwartz M
Univ. Kentucky Medical Center, Lexington, KY
Conn Med; 45(11):735-737 1981

Conclusions and recommendations regarding the tumor marker carcinoembryonic antigen (CEA) made during a Consensus Development Conference are presented. The upper limit of normal for CE A levels in plasma is 2.5 nanog/ml. Higher values may be associated with cancers (particularly of the gastrointestinal tract, pancreas, ovary, lung, and breast) but are also found in cigarette smokers, patients with benign tumors, and with inflammatory disorders, liver disease, and lung infections. CEA does not possess the sensitivity or specificity required to discriminate between localized malignant tumors and benign disorders. Grossly elevated values (5-10x normal), however, are strongly suggestive of cancer. Since preoperative CEA levels in patients with colorectal or possibly bronchial carcinomas can be indicative of survival rate, CEA values may be used in these cases in addition to clinical and pathological staging methods. Regular assay of CEA in postoperative colorectal cancer patients is the best method for detecting recurrence. The role of CEA in postoperative and therapeutic monitoring of other types of cancers is less convincing. Clinical utility of a tumor marker may be related to the efficacy of a therapeutic regimen. As more successful treatments for major tumor types become available, CEA and other tumor markers may become more useful in the management of cancer. (no Refs)

66. CARCINOEMBRYONIC ANTIGEN LEVELS IN THE DIAGNOSIS OF MALIGNANT LESIONS OF THE ABDOMINOPELVIC REGION.

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Dept. Obstetrics and Gynecology, Bronx-Lebanon Hosp. Center, New York, NY
Surg Gynecol Obstet; 153(5):693-696 1981

The differential diagnosis of tumors of the abdominopelvic region can be difficult. The inability to differentiate carcinoma of the colon and rectum from carcinoma of the ovary, in particular, may result in inadequate surgical procedures and unnecessary complications. In this study, elevated pretreatment levels of carcinoembryonic antigen were used as an aid in distinguishing between extragenital and gynecologic tumors in 76 women. Levels below 10 nanograms per ml suggested a malignant tumor of the female reproductive tract or benign disease; levels above 20 nanograms per ml indicated carcinoma of an extragenital organ. In addition to other diagnostic studies, pretreatment values of carcinoembryonic antigen may enable the physician to anticipate the specificity of the tumor and the scope of the surgical problem more precisely and, thus, be better able to prepare the patient for optimum treatment. (Author abstract) (8 Refs)

67. SERIAL DETERMINATION OF CARCINOEMBRYONIC ANTIGEN IN THE FOLLOW-UP OF PATIENTS WITH MALIGNANT TUMORS.

Eimermacher H, Schuster P, Beyer HK
Innere Abteilung, St.-Marien-Spital, Bergstr. 56, 5800 Hagen 1, W. Germany
Minerva Med; 72(48):3259-3262 1981

Fifty four patients with carcinomas (27 mammary, 12 bronchial, 3 ovarian, 3 uterine, 2 malignant lymphomas, 2 thyroid, 2 urinary vesicle, and one each stomach, esophagus, and skin) underwent serial carcinoembryonic antigen (CEA) determination. The patients were divided into three groups. Group A, was composed of 21 patients in remission following cytostatic, hormonal or irradiation therapy (IT). Group B, consisted of 16 patients who showed no improvement after different IT. Group C consisted of 17 patients who received no IT. The patients were observed for 2-18 mo. CEA controls were performed 2-12x. A good correlation was found between tumor growth and CEA levels. This was especially true for Group A patients. (8 Refs) (In ITA)

68. THE ROLE OF CARCINOEMBRYONIC ANTIGEN (CEA) AND OTHER TUMOR MARKERS.

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Istituto di Medicina Nucleare, Universita Cattolica, Roma, Italy
Radiol Med (Torino); 67(11):846-850 1981

Carcinoembryonic antigen (CEA) and other tumor markers are reviewed. The Bagshawe classification is presented. The clinical use of biological markers as controls after surgery, relapse, metastasis, follow up of therapy, and evolution of disease is discussed. In one study CEA was increased in 25% of early stage cancer patients and in 80% of advanced cases. Among 56 mammary cancer patients, CEA was increased in 35% before surgery, compared to only 13% 1-6 mo after surgery, with later increase to 73%. CEA determinations had a 73.3% sensitivity and an accuracy of 87%. Some promising experimental results have been obtained with the simultaneous determination of alpha-casein human chorionic gonadotropin, betahCG and CEA. Another study indicated the value in diagnosis of CEA, ferritin, reactive protein-C, plasma acid glycoprotein, alkaline phosphatase, sialotransferase and the hydroxyproline/creatinine ratio. (42 Refs) (In ITA)

69. A CASE OF PRIMARY YOLK SAC TUMOR OF THE THYMUS WHICH SHOWED HIGH LEVELS OF AFP, HCG, AND CEA AND REVIEW OF LITERATURE.

Arimura T, Baba K, Tanaka Y, Fukukami A, Mitani T, Takao T, Kawaita H, Nishi M, Nakakama H, Sonoda Y, Tanaka T
First Dept. Surgery, Kagoshima Univ. Sch. Medicine, Kagoshima, Japan
Nippon Kyoba Geka Gakkai Zasshi; 29(7):1233-1241 1981

A 21-yr-old male patient with a mediastinal (thymic) primary yolk sac tumor was reported, and the literature on primary mediastinal yolk sac tumors was reviewed. The patient had elevated levels of serum alpha-fetoprotein (AFP; 12,800 nanog/ml), human chorionic gonadotropin (88.1 milliIU/ml), and carcinoembryonic antigen (CEA; 4.1 nanog/ml). The patient died with recurrence 7 mo after surgical resection of the tumor and postoperative radio and chemotherapy. When the tumor recurred only the AFP and CEA levels increased. Seventeen cases of mediastinal yolk sac tumors were reported in the Japanese literature; the patients were 1 yr 5 mo to 54 yr old, and AFP levels were 25-169,700 nanog/ml. Sixteen cases were reported in Western literature; AFP levels in the patients (1 woman, 11 men, 4 unknown; 7-33 yr old) were 0-58,000 nanog/ml. (50 Refs) (In JPN)

70. DIAGNOSTIC APPLICATIONS OF ALPHA-FETOPROTEIN: GOVERNMENT REGULATIONS PREVENT FULL APPLICATION OF A CLINICALLY USEFUL TEST.

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Dept. Pathology, Sch. Medicine, Univ. California at San Diego, La Jolla, CA, 92093
Hum Pathol; 12(11):959-963 1981

An elevated serum concentration of alpha-fetoprotein (AF) in a nonpregnant adult is the single most discriminating laboratory test indicative of malignant disease. Elevations of the serum AF level above 400 nanog/ml are essentially diagnostic of hepatocellular cancer. Elevations of the serum AF level in experimental animals exposed to chemical hepatocarcinogens may be obvious many mo before the appearance of hepatocellular carcinoma. Elevations of serum AF following acute liver injury reflect the degree of liver cell regeneration. Germ cell tumors are associated with elevations of the serum AF. Low levels of serum AF may be associated with tumors of the gastrointestinal tract or lungs. Measurement of AF in maternal serum is an established procedure in parts of Europe as a means of screening for open neural tube defects. This application in the United States has been delayed by a peculiar set of circumstances involving government regulations and strong political lobbying groups. (5 Refs)

71. COLLABORATIVE STUDY ON BRONCHIAL TUMOUR-ASSOCIATED ANTIGENS.

Gennings JN, Bagshawe KD, Axelsen NH, Sizaret P
Dept. Medical Oncology, Charing Cross Hosp. (Fulham), London, W6 8RF, England
Br J Cancer; 44(4):487-495 1981

Eleven groups of workers submitted a total of 21 bronchial tumor-associated antigen preparations and 19 antisera for comparative studies. Many of the antisera proved to be polyspecific despite absorption procedures. Most of the antigen preparations contained some material reactive towards a reference antiserum to normal human serum proteins. White it appeared that no participants were studying identical antigen-antibody reactions, several cross-reactivities were identified in the antisera. When immune reactions to CEA, AFP, NCA, ferritin, lactoferrin, human pepsin and gastricsin, and the pregnancy proteins, SP1 and SP3 were excluded by use of reference antisera and electroimmunoprecipitation methods, there remained five antigen-antibody reactions defining unique antigens. The clinical usefulness of any of these five antigens has yet to be determined. (Author abstract) (14 Refs)

72. RELATIONSHIP BETWEEN SERUM ALPHA-FOETOPROTEIN, CIRRHOSIS AND SURVIVAL IN HEPATOCELLULAR CARCINOMA.

Johnson PJ, Melia WM, Palmer MK, Portmann B, Williams R
Liver Unit, King' Coll. Hosp. Medical Sch., Denmark Hill, London SE5, England
Br J Cancer; 44(4):502-505 1981

An analysis of survival time of 57 West European patients with hepatocellular carcinoma was carried out to define which of several possible factors (age, sex, cirrhosis and raised serum alpha-fetoprotein (AFP)) influenced survival. Although survival was significantly longer in younger patients (p less than 0.02) and in patients with normal serum AFP (p less than 0.01), multivariate analysis showed that significant variation in survival time is better explained by the single factor, the presence of cirrhosis, than by AFP level. This does not seem to apply for patients with this tumor in Africa and the Far East, and there may be a fundamental difference in the natural history of the tumor between high- and low-incidence areas. (Author abstract) (14 Refs)

73. PRE- AND POSTOPERATIVE CHANGES OF ALPHA-FETOPROTEIN AND HUMAN CHORIONIC GONADOTROPIN IN HEPATOMA OF CHILDREN.

Ikeda K, Kimura N, Suita S, Hayashida Y, Nakagawara A, Kawaoi A
Dept. Pediatric Surgery, Faculty Medicine, Kyushu Univ., 1-1, 3-chome Maedashi, Higashiku, Fukuoka 812, Japan
Z Kinderchir; 34(1):42-55 1981

Serial determinations of alpha-fetoprotein (AFP) and immunoperoxidase staining for AFP and human chorionic gonadotropin (HCG) producing cells were performed in 15 children (9 boys, 6 girls; age 4 mo to 11 yr, 5 mo) with malignant liver tumor (14 hepatoma, 1 undifferentiated sarcoma). Serial serum AFP determinations in nine patients revealed normal preoperative levels in two and levels of 150,000-2,500,000 nanog/ml in seven. Postoperative AFP changes were of three types: (1) transient decrease followed by gradual increase, as seen in patients treated by interruption of hepatic blood supply combined with chemotherapy, (2) rapid decrease in AFP level to near-normal followed soon after by increase, seen in patients with recurrence after resection, and (3) marked and consistent fall of AFP, found in patients with complete recovery after resection. In one patient with AFP and HCG producing hepatoblastoma, recurrence was associated with increase only in AFP. Immunoperoxidase staining of the resected specimen showed both AFP and HCG producing cells in a well-differentiated nest composed of distinctive cells constituting only part of the tumor. (10 Refs)

74. THE VALUE OF SERUM 5'-NUCLEOTIDE PHOSPHODIESTERASE ISOZYMES IN THE DIAGNOSIS OF PRIMARY LIVER CANCER.

Lu H, Chen Q, Jiang K, Ming D, Shi B, Ding C, Pan L, Yu J, Liu Z
Shanghai Second Medical Coll., Affiliated Xinhua Hosp., Shanghai, People's Republic of China
Zhonghua Yixue Zazhi; 60(4):219-221 1981

The use of alpha fetoprotein (AFP) determination has greatly increased the diagnostic level of primary liver cancer in recent yr. However, there is a small proportion of liver cancers that are negative for AFP. The value of serum 5'-nucleotide phosphodiesterase isoenzymes (NPI) in the diagnosis of liver cancers is described with special reference to those negative for AFP. Of 95 cases of primary liver cancer tested between 1979 and 1980, 79 cases (83.2%) were positive for NPI. Among 70 AFP-positive cases, 60 cases (85.7%) were NPI-positive and among 25 AFP-negative cases, 19 cases (76.0%) were NPI-positive. Among 15 resected cases of primary liver cancer only 2 cases (13.3%) were NPI-positive. Liver cirrhosis and HBSAG-positive hepatitis had a positive rate of 10.3% (4/39) while none of the 76 normal subjects tested was positive for NPI. It was concluded that NPI determination when combined with AFP determination is useful in the diagnosis of primary liver cancer as well as in its differential diagnosis from non-cancerous liver diseases. (7 Refs) (In CHI)

75. A STUDY OF SERUM CARCINOEMBRYONIC ANTIGEN (CEA) IN PANCREATIC CANCER.

Tomida T, Nenohi M, Goshima H, Kawarada Y, Mizumoto R
First Dept. Surgery, Sch. Medicine, Mie Univ., Tsu-shi, Mie Pref. 514, Japan
Nippon Shokaki Geka Gakkai Zasshi; 14(4):554-558 1981

The concentration of CEA in the serum was 2.5 ng/ml or more in 16 of the 23 patients with pancreatic cancer, and 5.1 ng/ml or more in 9 of these patients. However, only one of the five patients with carcinoma of the ampulla of Vater had a value of 2.5 ng/ml or more. All the five patients with carcinoma of the ampulla of Vater had CEA values of 5.0 ng/ml or less and their cancers could be resected. The cancers of seven patients with carcinoma of the head of the pancreas whose CEA value was 5.0 ng/ml or less could be resected, and except for one patient who had palliative resection, none of the cancers of the nine patients who had serum CEA values of 5.1 ng/ml or more could be resected. Of the 10 patients who had carcinoma of the head of the pancreas or carcinoma of the ampulla of Vater, and had arterial invasion limited to the arcade of the head of the pancreas, 8 had a serum value of 5.0 ng/ml or less, and all of the 8 patients excluding 1 with distant metastasis had resectable cancer. Of the six patients who had invasion into the gastroduodenal artery or superior mesenteric artery, four had CEA values of 5.1 ng/ml or more. The cancers of these four patients were not resectable while those of the remaining two were. All the patients who had Stage I-III pancreatic cancer according to Hermreck, and had CEA values of 5.0 ng/ml or less, had resectable cancer. Of the patients with resectable cancer, two of the four who had high preoperative serum CEA values had normal values on Days 6 and 10, but the values of the other two, who had palliative resection, did not return to normal. Except for two patients who had low preoperative serum CEA values, the patients with nonresectable cancer had gradually increasing CEA values and died. Therefore, the serum CEA value is a valuable method for determining the possibility of radical resection for pancreatic cancer and for prognosis. (16 Refs) (In JPN)

76. CARCINOEMBRYONIC ANTIGEN IN THE EVALUATION OF THE EFFICACY OF RADIOTHERAPY OF LUNG CANCER.

Dobrovol'skii NM, Medvedev VN, Firsova PP
Res. Inst. Medical Radiology, Obninsk, USSR
Med Radiol (Mosk); 26(10):22-25 1981

Blood level of carcinoembryonic antigen (CEA) was monitored in 46 patients undergoing radiotherapy for Stage II-III lung cancer. Prior to the radiotherapy, increased CEA level (greater than 10 ug/liter) was observed in 33% of the patients. The radiotherapy caused a progressive decrease in the CEA level. (11 Refs) (In RUS)

77. THE VALUE OF POLY-C-SPECIFIC SERUM RIBONUCLEASE AND CEA IN THE DIAGNOSIS OF PANCREATIC CARCINOMA.

Holbling N, Funovics J, Euler J, Karner J, Zoch G, Sauermann G
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Klin Wochenschr; 59(21):1201-1207 1981

The possible role of poly(C)RNase serum activity and CEA serum level for early detection and differentiation of pancreatic carcinoma and its specificity and valuability were critically analyzed: Serum RNase (median, min-max) with polycytidin as substrate was determined in 13 'normal' patients, 16 patients with pancreatic cancer, 15 patients with chronic pancreatitis, 7 patients with acute pancreatitis and 13 patients with other types of malignomas. Serum CEA level was evaluated in 18 'normal' patients, 12 patients with pancreatic carcinoma, 13 patients with chronic pancreatitis, 8 patients with acute pancreatitis and 5 patients without operative verification of suspected pancreatic carcinoma. The serum RNase activity in pancreatic cancer patients did not show any significant increase in comparison to the other groups, and these patients could not be distinguished from those with the other diseases when excluding other factors influencing serum RNase level such as: Renal insufficiency, nutrition, age, sex. Their CEA level was significantly higher in comparison to the other groups (p less than 0.05). Using 2.5 ng/ml as the limit, the sensitivity was found to be 80% (10/12 of pancreatic carcinomas positive) and the specificity being 70.5% (31/44 of other groups without malignant diseas negative). The present study and data in the literature show that poly (C) RNase measurement is not useful in early detection of pancreatic carcinoma, but the CEA test could be helpful in the differential diagnosis of pancreatic diseases due to its specificity (70.5%) and seems to be valuable in detection of residual and in monitoring for recurrent pancreatic carcinoma in view of its sensitivity and correlation with the stage of cancer. (20 Refs) (In GER)

ULTRASTRUCTURE/ CYTOCHEMISTRY

78. IMMUNOHISTOCHEMICAL DEMONSTRATION OF CARCINOEMBRYONIC ANTIGEN IN NORMAL, TRANSITIONAL AND INFLAMED COLONIC MUCOSA.

Wager C, Hain F, Breuer H, Olude S, Cremer H, Muller-Walraf R
Institut fur Klinische Biochemie, Universitat Bonn, Bonn, W. Germany
Oncodev Biol Med; 2(5):331-343 1981

The presence of carcinoembryonic antigen (CEA) in normal colonic tissue was demonstrated by immunohistochemistry using the peroxidase-antiperoxidase technique. In colorectal mucosa from the resection margins of colon carcinoma, CEA positive staining appeared on the surface epithelial cells. In those specimens showing a CEA positive staining in the crypt, the arrangement of crypts was regular. Compared with normal mucosa, the main features of colorectal mucosa adjacent to the carcinoma (transitional mucosa) were loss of parallelism, lateral budding and branching of crypts. The CEA positive staining was more intense than in the normal mucosa. In ulcerative colitis, intense CEA positive staining was observed in areas with regenerative activity and in precancerous and cancerous specimens. CEA specific staining intensity was highest in a section of colonic mucosa in ulcerative colitis showing marked dysplasia and in a colon carcinoma specimen. A low CEA specific staining intensity was observed in a poorly differentiated ulcerative colitis-associated carcinoma. It is suggested that pronounced membrane staining is more an indication of proliferation than of cancer or precancer. (30 Refs)

79. THE IMPORTANCE OF LECTIN BINDING SITES AND CARCINOEMBRYONIC ANTIGEN WITH REGARD TO NORMAL, HYPERPLASTIC, ADENOMATOUS, AND CARCINOMATOUS COLONIC MUCOSA.

Klein PJ, Osmers R, Vierbuchen M, Ortmann M, Kania J, Uhlenbruck G
Pathologisches Institut, Universitat Koln, Josef-Stelzmann-Strasse 9, D-5000 Koln 41, W. Germany
Recent Results Cancer Res; 79:1-9 1981

Lectin and carcinoembryonic antigen (CEA) binding sites were studied in normal and tumorous colonic mucosae. Tissue samples included 15 macroscopically normal margins from colonic carcinoma patients, 26 transitional mucosa samples, 3 hyperplastic polyps, 16 adenomas, and 33 colonic carcinomas of various degrees of differentiation. Normal and carcinomatous mucosae differed mainly in number of binding sites for various lectins and anti-CEA antibodies; staining was therefore not tumor-specific. Transitional mucosa had higher levels of lectin and CEA binding sites and higher production of mucinous substances than normal mucosa. Adenomatous mucosa exhibited similar characteristics, but lectin binding sites were reduced in proliferating areas. Lectin binding sites varied in number among carcinoma samples, increasing in partial relationship with the degree of tumor differentiation. CEA and Ricinus communis agglutinin binding sites frequently showed similar distributions in carcinoma samples. Peanut agglutinin binding sites were present only in transitional and carcinomatous mucosae. Results suggest that a disturbance in production or in composition of mucosal glycoproteins of the colon may reflect an initial phase of colonic cancer; lectins in the diet may affect cell proliferation, an essential factor of tumorigenesis. (25 Refs)

80. HISTOLOGICAL IDENTIFICATION OF CARCINOEMBRYONIC ANTIGEN IN BREAST CANCER. USE OF AN IMMUNOHISTOCHEMICAL TECHNIQUE IN 71 CASES OF BREAST CANCER.

Bonetti F, Maconi A, Pisa R, Menestrina F, Novelli P, Iannucci A, Chilosi M, Rasniewskij K
Istituto di anatomia, Universita di Padova, Verona, Italy
Pathologica; 73(1026):639-647 1981

A modification of the Burns technique using tagged antibodies and peroxidase was used in the determination of carcinoembryonic antigen (CEA). The CEA can be observed inside the cytoplasm as granules of variable size or as finely dispersed dust. This technique may also be used also in the retrospective study of prepared paraffin sections. Of the 71 infiltrating mammary carcinomas studied, 58 were positive and 13 negative. The CEA positive results were expressed as percent of CEA positive cells in relation to total number of neoplastic cells. The results varied according to histological type of mammary carcinoma (MC). Of 49 infiltrating ductal MC, 4 were negative, 8 showed 1-30%, 26 showed 30-70%, and 11 showed 70-100% positive cells. The results for 11 lobular infiltrating MC were 4, 5, 1, and 1, respectively. Of the 5 medullary MC, 2 were negative and 3 showed 70-100% positive cells. Of the 4 papillary MC, 2 were negative and 2 showed 30-70% positive cells. Of the 2 colloid MC, 1 was negative and 1 showed 1-30% positive cells. A larger sample is necessary to determine the significance of these results. (21 Refs) (In ITA)

81. LOCALIZATION OF TENNESSEE ANTIGEN BY IMMUNOHISTOCHEMICAL ANALYSIS OF NORMAL TISSUES AND CARCINOMA (MEETING ABSTRACT).

Ramsey R, Lovins R, Hokama Y
Lancer, Foster City, CA
Oncodev Biol Med; AbstractsBook,1:P4 1981

Tissue sections derived from carcinomas, normal tissue adjacent to the neoplastic site, and normal tissue from other sources were all examined for the presence of Tennessee Antigen and for carcinoembryonic antigen (CEA) using direct immunofluorescent techniques. Examination of the sections stained with labelled Anti-Tennessee Antigen serum demonstrated that the primary staining of the malignant tissue was associated with cell plasma membranes. Where cytoplasmic staining was observed, it was associated primarily with normal goblet cells which were interspersed within lesions. No appreciable staining of the inflammatory or necrotic tissue around lesions was observed. Faint membrane staining was associated with some of the normal tissues studied. The staining observed with malignant tissue using fluorescently labelled anti-CEA serum was similar to the pattern already described for Anti-Tennessee Antigen serum in that the anti-CEA staining was mainly of cell membrane of the tumor cells. Cross-inhibition studies demonstrated that unlabelled anti-CEA serum did not inhibit staining for Tennessee Antigen by fluorescently-labelled Anti-Tennessee Antigen serum. Conversely, unlabeled Anti-Tennessee Antigen serum did not inhibit the staining by the labelled Anti-CEA serum, indicating that the two antigens are structurally different and possess distinct immunochemical specificities. (no Refs)

82. ASSESSMENT OF BIOCHEMICAL DIFFERENTIATION OF BREAST CANCER USING BIOLOGICAL MARKERS OF MALIGNANCY (MEETING ABSTRACT).

Panko WB, Silvers A
Department of Pathology, Baylor College of Medicine, Houston, TX, 77030
Oncodev Biol Med; AbstractsBook,1:59 1981

We have attempted to gain insight into the biological characteristics of individual breast cancers by determining the presence or concentration of biological markers of malignancy in the cytosol in 199 breast cancers and relating these findings to steroid hormone receptor concentrations. The biological markers measured were carcinoembryonic antigen (CEA), the beta subunit of human chorionic gonadotrophin (beta-hCG), and alpha-fetoprotein (AFP). Estrogen and progesterone receptor (ER and PgR) were chosen because there is evidence that they are independent indicators of differentiation. AFP was detected in only 2 of 199 tumors, though there are recent reports that AFP is non-immunoreactive in breast cancer. Using a modified beta-hCG radioimmunoassay (RIA), 90% of breast cancers were found to contain detectable levels of beta-hCG. CEA was also found in most breast cancers, though the distribution of CEA concentrations appeared to be bimodal. Linear regression analysis did not indicate any significant degree of association of CEA or beta-hCG to ER or PgR, or to each other. However, tumors which were in the top quartile with respect to CEA concentration had higher than av ER concentrations but less than av PgR concentrations. This finding suggests that there may be a biochemical defect in those tumors with high CEA levels that prevents estrogen induction of PgR. (no Refs)

83. ECTOPIC PRODUCTION OF ONCODEVELOPMENTAL PROTEINS BY BREAST CANCERS (MEETING ABSTRACT).

Horne CH, Bremner RD, Nisbet AD, Bohn H, Ratcliffe JG
Department of Pathology, University of Aberdeen, Aberdeen, Scotland
Oncodev Biol Med; AbstractsBook,1:P66 1981

Using an indirect immunoperoxidase technique and specific sensitive radioimmunoassays a series of breast cancers sent to this laboratory for routine frozen section diagnosis have been screened for the presence of pregnancy-specific glycoprotein (SP1), placental protein five (PP5) and carcinoembryonic antigen (CEA). In addition the occurrence of these oncodevelopmental proteins has been compared with the presence or absence of estrogen receptors. (no Refs)

84. ROLE OF THE INTERMEDIATE CELL IN MALIGNANT DISEASE OF THE UPPER GASTROINTESTINAL TRACT (MEETING ABSTRACT).

Jass JR
Westminster Medical School, London SWIP 2AR, England
J Clin Pathol; 34(7):817 1981

A combined morphological, histochemical, and immunohistological study was carried out on the epithelium bordering adenocarcinomas of both the esophagus (32 cases) and stomach (48 cases). Benign specimens including 25 gastrectomies (selected to show intestinal metaplasia) and 10 esophageal biopsies (selected to show the columnar epithelium of Barrett) served as controls. The material was formalin-fixed and both conventional and semithin sections were prepared. These were stained with hemotoxylin and eosin, PAS-Diastase, Alcian Blue (AB)/PAS and High Iron Diamine/AB. The latter two sequences permitted distinction between neutral and acid mucins and sulpho- and sialomucins respectively. Sections from eight cases of esophageal adenocarcinoma were stained for carcinoembryonic antigen (CEA) by an immunoperoxidase technique. Columnar epithelium (Barrett's esophagus) was present in 19 of the esophageal adenocarcinomas. In these as well as the gastric cases an unusual 'intermediate' columnar cell was commonly observed showing features of both absorptive cell and a mucous cell. CEA reactivity was present along the brush border of mature absorptive cells but in the apical cytoplasm of certain intermediate cells secreting minimal amounts of mucus. There was an association between intermediate cells secreting sulphomucins and well differentiated adenocarcinomas in both the stomach and esophagus. Mature absorptive cells - that is, complete intestinal metaplasia were common in both benign and malignant specimens. Hyperplasia of the intermediate cells has also been described in metaplastic polyps of the colon and the transitional mucosa bordering colonic carcinomas and is clearly an ubiquitous disorder of growth and differentiation. (no Refs)

85. LOCALIZATION AND MORPHOLOGICAL OBSERVATION OF ENZYME-LABELLED IMMUNOFETOPROTEIN IN HUMAN LIVER CANCER AND PERICANCEROUS LIVER TISSUE.

He D, Dai Y, Tao W, Wang H, Wu g, Ping B, Zheng B
Dept. Pathologic Anatomy, Second Military Medical Coll., People's Republic of China
Zhonghua Yixue Jianyan Zazhi; 4(1):12-16 1981

In recent yr, the distribution of alpha-fetoprotein (AFP) in liver cancer and its relationship to hepatocarcinogenesis has been reported. However, the distribution of AFP in pericancerous

cerous liver tissue in primary hepatoma patients has not been reported. Results of AFP distribution studies are described for 22 cases of primary hepatoma (17 males, 5 females), using an indirect enzyme-labeled antibody technic. Surgical liver specimens were used. It was found that AFP was distributed mainly in the cytoplasm of cancer and pericancerous cells. The distribution was mostly diffused, with only a small portion localized in a particular part of the cytoplasm, beneath the cell membrane or around the nucleus. Tissue distribution of AFP was random, with most AFP-positive cells located at the edge of the cancer mass, in the lobule and around intrahepatic veins. In most cases, AFP-positive rate was higher in pericancerous cells than in liver cancer cells and was related to the activity of chronic liver diseases. (15 Refs) (In CHI)

REVIEWS/ OTHER RELATED STUDIES

86. HEPATOCELLULAR CARCINOMA IN 1981.

Sherman M, Terblanche J, Kirsch RE
UCT-MRC Liver Res. Group, Dept. Medicine, Univ. Cape Town Medical Sch., Observatory, Cape, South Africa
S Afr Cancer Bull; 25(1/2):31-33 1981

Incidence, course, diagnosis, and treatment of hepatocellular carcinoma (HCC) in South Africa are discussed. HCC shows definite geographic and racial variation in incidence, is identifiable by the presence of alpha-fetoprotein (AFP), and may present different clinical courses. Factors related to development of HCC include aflatoxin and hepatitis B virus (HBV). In South Africa HBV infection occurs at an early age in rural Blacks, possibly explaining why these patients develop HCC as early as the third decade. Patients with hemochromatosis and cirrhosis also have an increased risk of HCC. In South African Blacks, HCC is a fulminant rapidly fatal disease. Peak age of onset is the third and fourth decades as compared with the fifth and sixth decades elsewhere. Few South African Blacks survive greater than 1 yr from the time of diagnosis; death is usually due to the tumor rather than underlying liver disease. AFP levels greater than 1,000 nanog/ml are usually diagnostic of HCC. AFP is elevated in greater than 95% of South African Black patients and levels greater than 1,000 nanog/ml are found in greater than 60%. Several invasive and non-invasive methods for detection of this tumor are described. The only certain curative therapy is resection of the affected lobe when the underlying liver is normal and the tumor is confined to a single lobe. In most South African patients, this is very unusual and most HCC are inoperable. Among Coloreds, resectability is higher, but still low. Liver transplants have been performed for HCC, but many patients have died from metastases. Chemotherapy or radiotherapy for African HCC is of little value. (4 Refs)

87. INITIATION AND CHARACTERIZATION OF CULTURES OF HUMAN COLONIC CARCINOMA WITH DIFFERENT BIOLOGICAL CHARACTERISTICS UTILIZING FEEDER LAYERS OF CONFLUENT FIBROBLASTS.

Brattain MG, Brattain DE, Fine WD, Khaled FM, Marks ME, Kimball PM, Arcolano LA, Danbury BH
Dept. Biochemistry, Univ. Alabama, Birmingham, AL, 35294
Oncodev Biol Med; 2(5):355-366 1981

The effects of feeder layers of C3H 10 1/2 murine fibroblast cells on the establishment of cultures of human colonic carcinoma were determined for 27 tumor specimens. Of the 27 specimens, 21 were successfully established on feeder layers. All except for 1/21 have been sub-cultured at least 10 times and have been maintained in tissue culture for 6-12 mo. When feeder layers were not used only three specimens were able to grow and survive passage in culture. Of the 21 specimens grown in long-term cultures, 14 have been weaned from fibroblasts and characterized. These 14 lines were divided into three groups on the basis of their tumorigenicity in nude mice. Group 1 cells, in general, produced poorly differentiated tumors and had in vitro morphologies typical of the grape-like cluster or miscellaneous forms. Group 2 cells were less tumorigenic than Group 1 cells, they grew poorly or not at all in semi-solid medium and produced carcinoembryonic antigen (CEA) levels in the medium of confluent cultures that were indistinguishable from those of Group 1 cells. Tumors from Group 2 cells were differentiated and, in general, grew in an epithelioid pattern in vitro. Group 3 cells were, in general, not tumorigenic, produced large amounts of CEA, grew in the epithelioid pattern, and would not grow well in semi-solid medium. (28 Refs)

88. CHEMICAL AND X-RAY INDUCED ANTITUMOR CELL-MEDIATED CYTOTOXICITY TO RAT FETAL CELLS (MEETING ABSTRACT).

Cheng HF, Stevens RH, Cole DA
Radiation Research Laboratory, Department of Radiology, University of Iowa, Iowa City, IA, 52242
Oncodev Biol Med; AbstractsBook,1:P20 1981

Our recent studies have indicated the presence of a common oncofetal protein (OFP) occurring in rat tumors induced in the (i) small bowel by x-rays, (ii) colon by 1,2-dimethylhydrazine, and (iii) pancreas by 7,12-dimethylbenz[a]anthracene. Measurements of the antitumor cell-mediated immune (CMI) responses of these tumor-bearing rats revealed that the peripheral blood lymphoid-cells (PBLC) expressed cytotoxicity only to entodermal tissue derived tumor target cells and not to target cells from mesodermal or ectodermal tumors. The present series of studies were carried out to determine whether such PBLC would express cytotoxicity towards normal fetal targets, thus suggesting fetal components play a role in the education of the PBLC. CMI was determined by the release of peripheral and integral radioiodinated membrane proteins of primary fetal cells derived at stage of 16-18 day gestation from the intestine, skin and whole fetus. Positive CMI was observed for PBLC obtained from the rats having the small bowel, colon, and pancreas tumors expressed to the intestine and whole fetus. While these results do not unequivocally establish an immune role for the OFP they suggest there must be some common feature of the fetal cells with that of the tumor. (no Refs)

89. DIMETHYLSULFOXIDE-INDUCED MODIFICATION OF ONCODEVELOPMENTAL (AFP) AND LATE-DIFFERENTIATION (ALBUMIN) GENE EXPRESSION IN AN ESTABLISHED LINE OF MOUSE HEPATOMA CELLS (MEETING ABSTRACT).

Higgins PJ
Memorial Sloan-Kettering Cancer Center, 1275 York Avenue, New York, NY, 10021
Oncodev Biol Med; AbstractsBook,1:30 1981

The effect of the differentiation-inducing agent dimethylsulfoxide (DMSO) on the synthesis of alpha-fetoprotein (AFP) and albumin (ALB) was evaluated using in vitro-propagated mouse hepatic tumor cells (BW77-1). DMSO-treated cells exhibited increased intra- and extra-cellular accumulations of both proteins compared to control cultures. The ALB contribution to total cellular protein increased with exposure of BW77-1 cells to progressively higher concentrations of DMSO in the growth medium. In contrast, while a considerable enhancement in hepatoma cell-associated AFP was noted upon incubation in 0.5% DMSO compared to non-DMSO-treated hepatocytes (65% increase), the AFP content in total cellular protein declined slightly upon exposure of BW77-1 cells to DMSO in final concentrations of more than 0.5%. Inhibition of the in vitro expression of certain growth properties ascribed to the transformed state as a consequence of exposure of BW77-1 cells to increasing levels of DMSO in the growth medium was found to be correlated with changes in the progression of the hepatoma cell population through the cell cycle and with a gradually enhanced capacity for synthesis of a differentiated hepatocyte gene product (ALB) and concomitant restricted expression of an oncodevelopmental antigen (AFP). (no Refs)

90. INHIBITORY EFFECT OF THE PROTEIN SYNTHESIS BY ALPHA-FETOPROTEIN IN A RETICULOCYTE LYSATE CELL FREE SYSTEM (MEETING ABSTRACT).

Aoyagi Y, Takahashi Y, Odani S, Ogata K, Ono T, Ichida F
Departments of Internal Medicine, Niigata University School of Medicine, 757 Asahimachi-Dori-1, Niigata, 951, Japan
Oncodev Biol Med; AbstractsBook,1:30 1981

Protein synthesis (incorporation of 3[H]-leucine into the protein fraction) in a reticulocyte lysate cell-free system was inhibited by hepatoma-derived alpha-fetoprotein (AFP) in a dose-dependent fashion, and in the presence of 40 uM hepatoma-derived AFP it decreased to only about 15% of the control level (without AFP). An almost identical result was obtained when fetal AFP was added to the cell-free system. Serum albumin, purified from fetal cord sera, showed little inhibitory activity. The observed activity was not due to contamination by ribonuclease in the AFP preparation. It is tempting to regard this inhibitory action as a regulatory role of this embryonic protein. (no Refs)

91. AFP AND ALBUMIN EXPRESSION IN LIVER CELL HYBRIDS (MEETING ABSTRACT).

Gingras MC, Belanger L, Szpirer J, Szpirer C
Molecular Oncology Laboratory, Laval University, Quebec City, Quebec, Canada
Oncodev Biol Med; AbstractsBook,1:P7 1981

We have followed the secretion of alpha fetoprotein (AFP) and albumin by hybrid cells obtained from the fusion of mouse hepatoma cells BWTG3 with either rat Morris hepatoma 7777 cells or normal fetal rat hepatocytes. Cells were fused with Sendai virus, hybrids were selected and proteins were measured with specific radioimmunoassays. Mouse AFP production was maintained in both types of hybrid but it was lower in fetal hepatocyte x BWTG3 hybrids. Hybrids (7777 x BWTG3) secreted sizable amounts of rat albumin, suggesting that the 7777 cell line has a post-translational defect of albumin secretion. Rat AFP was maintained in the majority of hepatoma x hepatoma hybrids but infrequently in fetal hepatocyte x hepatoma hybrids. This suggests a greater karyotypic or phenotypic stability of AFP expression in malignant hepatocytes than in normal fetal hepatocytes. However, it also shows that the AFP function can be immortalized from a normal genome. In fetal hepatocyte x BWTG3 hybrids, the expression of rat AFP and rat albumin was not coordinated. (no Refs)

92. EXPRESSION OF ALPHA-FETOPROTEIN AND ALBUMIN GENES IN A RAT HEPATOMA CELL LINE SY/1/80: EVIDENCE FROM THE NEED OF SPECIES SPECIFIC SERUM FACTORS.

Selten GC, Selten-Versteegen AM, Yap SH

Dept. Medicine, St. Radboud Hosp., Univ. Nijmegen, 6500 HB Nijmegen, The Netherlands

Biochem Biophys Res Commun; 103(1):278-284 1981

The requirement for rat serum factors to express the alpha-fetoprotein (AFP) and albumin genes in rat hepatoma cell line SY/1/80 is reported. SY/1/80 is a cell line derived from a diethylnitrosamine-induced rat hepatoma. The original tumor produces both AFP and globin protein. During in vitro passage of cells in medium supplemented with calf, horse or human serum, the mRNAs for these proteins could not be detected. Supplementation of cultures with rat serum induced the appearance of both AFP and globin mRNAs. While the nature and mechanisms of such species-specific serum factors remains to be elucidated, this observation may explain the inability of cells passaged in calf serum to produced specific proteins in a continuous fashion. (19 Refs)

93. IMMUNOPRECIPITATION ASSAY OF ALPHA-FETOPROTEIN SYNTHESIS BY CULTURED MOUSE HEPATOMA CELLS TREATED WITH ESTROGENS AND GLUCOCORTICOIDS.

Rosebrock JA, Parker CL, Kute TE

(c/o Parker) Dept. Biology, Atlanta Univ., Atlanta, GA, 30314

Differentiation; 19(3):168-178 1981

This investigation was to study the biosynthesis of 3H-labeled alpha-fetoprotein (AFP) by cultured mouse hepatoma (HEPA-2) cells. Both the function and regulation of this oncodevelopmental gene are unknown. However, evidence indicates that mechanisms controlling the expression of AFP involve aspects of both normal embryonic development and neoplastic transformation. The secretion of AFP was an alyzed during different phases of the growth cycle to provide information on AFP production using standard culture conditions. the highest rate of secretion occurred during the stationary phase, followed by the late logarithmic and early logarithmic phases of growth, respectively. The production of AFP was then determined following the addition of glucocorticoids and estrogens in an attempt to understand hormonal factors that may be involved. Studies utilizing estradiol-17beta indicated that the secretion of AFP did not appear to be sensitive to this steroid even though sucrose density gradient analysis of HEPA-2 cytosol, for estrogenic receptors, revealed competitive binding moieties in the 8S and 4S regions of the gradient. In contrast, the secretion of the total complement of proteins, including AFP, was significantly stimulated by the glucocorticoids, dexamethasone and corticosterone. Analysis of HEPA-2 cytosol for glucocorticoid receptors revealed binding components in the 7S and 3-4S regions of the gradient. The 3H-dexamethasone binding appeared to be stereospecific since nonlabeled dexamethasone, but not nonlabeled estradiol-17beta, effectively displaced the bound radioactivity. The glucocorticoid-binding component in HEPA-2 therefore displayed characteristics reported for glucocorticoid receptors in normal liver and other hepatomas. (Author abstract) (69 Refs)

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STRUCTURE/ IDENTIFICATION/ CHARACTERIZATION

1. MONOCLONAL ANTIBODIES TO HUMAN PROSTATE AND BLADDER TUMOR ASSOCIATED ANTIGENS (MEETING ABSTRACT).

Starling JJ, Wright GL

Eastern Virginia Medical School, Norfolk, VA, 23501

Hybridomas and Cellular Immortality (Second Houston Symposium), November 5-6, 1981, Houston, Texas. University of Texas Medical School at Houston 55 pp., 1981.

Monoclonal antibodies to human prostate adenocarcinoma membrane antigens were produced by fusion of spleen cells from Balb/C mice immunized against the prostate cancer cells line DU145, and the P3X63/Ag8 mouse myeloma line. The hybrids were screened for antibody production using glutaraldehyde-fixed or live cells in an in vitro binding radioimmunoassay (RIA). Antibody binding specificity was also checked by quantitative adsorption studies. A hybridoma clone (83.21) was isolated that secreted antibodies which preferentially bound to prostate and bladder cancer cells but did not bind to a variety of other normal and malignant human cell lines. This antibody

HE 20.3173/2:

also reacted with a cytomegalovirus-transformed human embryonic lung cell line but not to normal human embryonic lung cells. Conventional and competitive binding studies indicate that the 83.21 monoclonal antibody does not bind to alpha-fetoprotein, carcinoembryonic antigen, prostatic acid phosphatase, human WBC antigen (HLA), beta2 microglobulin, fibronectin, prostate specific antigen or DR antigens. Preliminary immunoprecipitation data with 125I-labeled, detergent soluble, DU145 membrane proteins and the 83.21 monoclonal antibody suggest that this antibody binds two proteins with mol wt of 210 and 97 kilodaltons. (no Refs)

ASSAY PROCEDURES/ SYNTHESIS

2. AN IMPROVED PROCEDURE FOR ISOLATION OF RAT ALPHA-FETOPROTEIN.

Ali M, Balapure AK, Durani S, Sahib MK
Div. Biochemistry, Central Drug Res. Inst., Lucknow 226 001, India
Indian J Biochem Biophys; 18(2):105-109 1981

A simple, two-step procedure for isolation of alpha-fetoprotein (AFP) from rat amniotic fluid is described. The procedure, which involves negative immunoabsorption and diethylaminoethyl cellulose chromatography, is more rapid and gives a higher yield (about 87%) than conventional procedures. Polyacrylamide gel electrophoresis resolved AFP into two variants with close mobility and which possessed a common antigenic determinant site and immunologic cross reactivity. (37 Refs)

3. THE COMBINED USE OF CARCINOEMBRYONIC (CEA) AND EPITHELIAL MEMBRANE ANTIGEN (EMA) FOR THE FLOW-CYTOMETRIC IDENTIFICATION OF TUMOR CELLS IN CERVICAL SMEARS (MEETING ABSTRACT).

Valet G, Ormerod M, Warnecke H, Benker G, Ruhenstroth-Bauer G
Max-Planck-Institut fur Biochemie, D-8033 Martinsried, W. Germany
VIII Conference on Analytical Cytology and Cytometry, May 19-25, 1981, Wentworth-by-the-Sea, New Hampshire Memorial Sloan-Kettering Cancer Center; 1981

Antigenic markers as carcinoembryonic antigen (CEA) or epithelial membrane antigen (EMA) are useful tools for the identification of tumor cells in tissue sections. We have performed simultaneous three parameter measurements (cell vol, DNA, antigen) with a FLUVO-METRICELL flow cytometer on single cell suspensions of human tumors of the cervix uteri, the colon and the breast using affinity purified monospecific antisera against CEA and EMA antigenic determinants. The advantage of the three parameter measurement is first: that the sensitivity of detection of abnormal cells is increased by a factor of 20 to 30 compared with a two parameter measurement, and second: that the labelled antigen on morphologically intact cells in different cell cycle phases can be well distinguished from unspecific binding of antibody to cell debris. The ratios of CEA to EMA antigen expression is variable from tumor to tumor. This may be of prognostic value for the patient and is also important because the measurement of both antigens increases the sensitivity of the method and decreases the rate of false negative samples. All tumors were recognized in a recent series of 25 cervical tumors and 20 normal smears. One normal sample was marginally false positive. It is likely that the sensitivity of the method can be further increased by the use of monoclonal antibodies. (no Refs)

IMMUNOLOGIC INTERACTIONS

4. DEPRESSED CELLULAR IMMUNITY IN HEPATOCELLULAR CARCINOMA PATIENTS.

Lee CS, Chang KJ, Lin TY, Hsieh KH, Tung TC
Dept. Surgery, Coll. Medicine, Natl. Taiwan Univ., Taipei, Taiwan
Taiwan I Hsueh Hui Tsa Chih; 80(8):780-785 1981

The techniques of sheep RBC rosette formation (E rosettes) and sheep RBC-antibody-complement formation (EAC rosettes) were used to study lymphocyte subpopulations in 40 patients with hepatocellular carcinoma (HCC) and in 120 age- and sex-matched normal controls. In the peripheral blood, E rosette-forming T cells comprised 49.18 +-10.92% of the lymphocytes from HCC patients compared to 72.00 +-11.50% in controls (p less than 0.001). EAC rosette B cells comprised 24.0% of the lymphocytes in both groups. The mitogenic index in the phytohemagglutinin-stimulated lymphocytes of 20 HCC patients was 12.26 +-17.82 (range 0.80-35.40) compared to 83.00 +-21.70 (range 18.00-124.80) in 40 controls. Serum alpha-fetoprotein (AFP) was determined in the 40 HCC patients. In the 28 with positive response, T cell count was 50.68 +-10.40% compared to 45.67 +-12.31% in 12 with negative response. The difference was not significant. Among 20 HCC patients tested for lymphocyte transformation, serum AFP was positive in 13 and negative in 7; mitogenic indices were 16.39 +-20.77 and 4.59 +-6.11, respectively. The difference was not significant. The significance of the low T cell count in peripheral blood of HCC patients is discussed. (16 Refs)

5. STUDY OF THE IMMUNITY MEDIATED BY CELLS IN 291 PATIENTS WITH MALIGNANT GENITOURINARY TUMORS.

Glait HM, Scorticati C, Feierstein JN, Bellora O, Koss A, Olivari AJ
Centro Oncologico de Medicina Nuclear, Instituto de Oncologia 'Angel H. Roffo', Buenos Aires, Argentina
Radiodiagn Radioter; 1(2):51-73 1981

Immunological states of 291 patients (14-88 yr old) with malignant genitourinary tumors (MGUT) were evaluated. Changes in the MGUT patients after hormonal treatment and radiotherapy were analyzed and were compared with changes in 27 patients that had benign urinary disease (BUD). The locations of the tumors were as follows: bladder (99), prostate (80), testicle (55), penis (20), kidney (28), and multiple (9). The following immunologic tests were performed: 2,4-dinitrochlorobenzene (DNCB), Can dida antigen (CA), streptokinase-streptodornase (SK/SD), phytohemagglutinin (PHA), alpha-fetoprotein (AFP), carcinoembryonic antigen (CEA), and circulating immune complexes (CIC). Every 3 mo different follow-up tests were performed depending on the location of the disease. The results for the BUD patients were as follows: DNCB (25 ug) positive (pos) in 48.1%, DNCB (100 ug) pos in 85.2%, CA pos in 48%, SK/SD pos in 59.3%, and blastic transformation normal in 68.4%. These results were lower than those for normal healthy persons. The results for the malignant tumor patients were presented according to location of tumor, stage of tumor, clinical evolution, use of radiotherapy, use of hormonal treatment, and histology (only in the cases of testicular seminoma). Correlation was observed between immunologic state and the evolution of the disease; this was most clearly demonstrated in non-patients with seminoma malignant tumors of the testicle, for whom the evolution of the disease and early diagnosis of relapse or metastases could be monitored. (36 Refs) (In SPA)

6. STUDIES ON CELL-MEDIATED IMMUNITY IN PATIENTS WITH COLORECTAL CANCER: LEUKOCYTE MIGRATION INHIBITION TEST (LMIT) USING ALLOGENEIC 3 M KCL EXTRACTS.

Kitagawa N
First Dept. Surgery, Kyoto Prefectural Univ. Medicine, Kamigyo-ku, Kyoto 606, Japan
Kyoto Furitsu Ika Daigaku Zasshi; 90(6):473-483 1981

The cellular immune response to tumor-associated antigens (TAA) had been monitored in patients with malignant tumors. In the present study, WBC from patients with colorectal and other malignant and nonmalignant gastrointestinal diseases and from normal subjects were tested by the LMIT, utilizing five different allogeneic 3 M KCl soluble extracts of colorectal cancer tissues. The normal range of the migration index (MI) was found to be 0.82 to 1.20 by calculating the mean MI +-2 SD (standard deviation) of 10 normal subjects. MIs out of this range were considered to be pathologic. In the LMIT with a single tumor extract, pathologic MI was found in 49.3% of 71 colorectal cancer patients, significantly higher than the 12-15% of other patients. In the panel method, ie testing each blood sample with five different tumor extracts, 78.9% of the patients with colorectal cancer were reactive, while 15% of gastric cancer patients showed positive reactions and no reactivity was observed in another group of patients. The difference between the colorectal cancer patients and the other patients was statistically significant. The frequency of positive reactivity was not related to the carcinoembryonic antigen value in the extracts. Markedly depressed reactivity was seen 10-14 days after curative resection, and in patients without recurrence the MI was normal during the 1-2 mo after surgery. However, positive reactions recurred in patients with local recurrence. Thus, the LMIT, particularly when tested by a panel method, seems to detect cell-mediated immunity against TAA of colorectal cancer. (28 Refs) (In JPN)

7. POSTOPERATIVE FOLLOW-UP OF NATURAL KILLER CELL ACTIVITY AND CEA IN PATIENTS WITH GASTROINTESTINAL CARCINOMA (MEETING ABSTRACT).

Betzler M, Quentmeier A, Geisenhainer U, Flad HD, Herfarth C
Department of Surgery and Microbiology, University of Ulm, Ulm, W. Germany
UICC Conference on Clinical Oncology, October 28-31, 1981, Lausanne, Switzerland. International Union Against Cancer 131 pp., 1981.

Recent studies have provided much evidence for the antitumor effect of Natural Killer (NK) cells. In this study it was examined, if the pre- and postoperative follow-up of NK cell activity shows a correlation to the carcinoembryonic antigen (CEA) level and the stage and the course of the disease. In 24 patients with gastrointestinal carcinoma the NK cell activity and the CEA serum concentrations was measured pre- and 4-8 wk postoperatively. In 10 patients multiple determinations could be performed up to 15 mo postoperatively. NK cell activity has been measured by a 51Cr release assay employing the human cell line K562. CEA serum concentration has been determined by radioimmunoassay. In 20/24 patients a positive correlation of the change of the NK cell activity, the CEA curve and the clinical stage of the disease was found. In potentially curative operated patients an increase of NK cell activity and a normalization of CEA values could be seen, in patients with tumor progression vice versa. By long term follow-up of both parameters we found even a higher positive correlation. Whether the NK cell activity or the CEA test is the more sensitive indicator concerning the early detection of tumor recurrence has to be examined in further studies. (no Refs)

8. EFFECT OF PLASMA EXCHANGE ON BLOCKING SERUM FACTORS IN PATIENTS WITH ADVANCED CANCER (MEETING ABSTRACT).

Schuff-Werner P, Beyer JH, Nagel GA
Division of Oncology and Department of Medicine, University Clinics, Robert-Koch-Str. 40, D-3400 Goettingen, W. Germany
UICC Conference on Clinical Oncology, October 28-31, 1981, Lausanne, Switzerland. International Union Against Cancer 131 pp., 1981.

In advanced cancer blocking serum factors (BSF) may influence host-tumor defense mechanisms thus promoting tumor growth and metastases. We report efforts first to demonstrate the presence of BSF and second to monitor for BSF before and after plasma exchange in cancer patients. A panel of cell culture assays was used to check for BSF. Eleven patients with malignant lymphoma and solid tumors refractory to conventional chemotherapy were studied. In all patients blocking serum activity as assessed by inhibition of mitogenic and allogenic lymphocyte stimulation could be removed by repeated or single plasma exchange. In order to gain some information about the nature of such BSF, results of cell culture assays were correlated with the behavior of acute phase reactants, oncofetal antigens and immune complexes. Results indicate that alpha1 antitrypsin may be one of the main inhibitors in Hodgkin's Disease and alpha2 macroglobulin seems to be correlated to suppressive serum activity in advanced breast cancer. (no Refs)

CLINICAL/ DIAGNOSIS/ IMMUNOTHERAPY

9. PROGNOSTIC SIGNIFICANCE OF CEA IN COLORECTAL CANCER: A STATISTICAL STUDY.

Persijn JP, Hart AA
Ziekenhuis Amsterdam-Noord, NL-1031 XP Amsterdam, The Netherlands
J Clin Chem Clin Biochem; 19(11):1117-1123 1981

Pretreatment and serial posttreatment levels of carcinoembryonic antigen (CEA) were studied in the sera of 222 patients with colorectal cancer; 205 patients underwent surgery as the primary treatment. Posttreatment levels during the subsequent 6 yr were expressed in actuarial or cumulative plots in relation to tumor-free period, time of diagnosis of recurrence, and time of diagnosis in local and distant recurrences. While pretreatment levels of CEA were significantly elevated, they gave no more prognostic information than that provided by the Dukes classification. Tumor-free periods of Dukes B patients were not significantly different if grouped according to different levels of their pretreatment CEA values. Among 144 patients with pretreatment values greater than 4.9/liter, 20 had residual tumor; two of these patients had CEA values which decreased to less than 5.0/liter within 100 days despite residual tumor, suggesting the possibility of a 'false' decrease. Pretreatment CEA values only had prognostic value in inoperable patients. Elevated pretreatment CEA did not exclude the possibility of curative treatment. Normalization of CEA after surgery did not indicate completeness of cure. In patients with local or distant recurrences, CEA in some instances rose before recurrences became clinically apparent. In approx 40% of patients, clinical diagnosis of recurrence preceded a rise in CEA. Max negative lead time was 385 days. Recurrence without a rise in CEA was exceptional. Results strongly suggest that serial CEA determinations cannot replace physical examination and follow-up. (28 Refs)

10. POSTOPERATIVE SCREENING OF PATIENTS WITH CARCINOMA OF THE COLON.

Beart RW, Metzger PP, O'Connell MJ, Schutt AJ
Mayo Clinic, Rochester, MN, 55905
Dis Colon Rectum; 24(8):585-588 1981

A prospective evaluation of 149 patients with Dukes' B2 or C colorectal carcinoma, including periodic history, physical examination, chest radiograph, liver function tests, complete blood count, carcinoembryonic antigen (CEA) radioimmunoassay, barium enema, and endoscopic studies, has been underway since 1976. Thirty-four patients have had recurrence. This study suggests that the history and CEA are the most sensitive noninvasive methods with which to detect recurrent tumors but are unlikely to indicate recurrence at a therapeutically advantageous stage. (Author abstract) (14 Refs)

11. PERSISTENT AND MARKEDLY ELEVATED CIRCULATING CARCINOEMBRYONIC ANTIGEN, WITHOUT EVIDENCE OF CANCER.

Bonard EC, Mach JP
Grand-Rue 19, CH-1315 La Sarraz, Switzerland
Schweiz Med Wochenschr; 111(48):1845-1849 1981

A markedly elevated circulating CEA level was observed in January 1978 in a 40-yr-old male patient who complained of functional digestive disorders consisting of 2-3 bowel movements at the end of each night. During follow-up of more than 3 yr the CEA level was always found to be higher than 300 ng/ml as determined on 12 different blood samples using 3 different assays: the Hansen assay, our own inhibition radioimmunoassay performed on perchloric acid extract of serum, and a newly developed solid phase non-competitive enzyme immunoassay involving monoclonal anti-CEA antibody. The clinical evolution showed no aggravation of the persistent but mild bowel troubles, ie no real diarrhea or blood in the stool. The patient enjoys excellent general health and shows no wt loss. Barium enema, colonoscopy and extensive investigation by computerized axial tomography showed no evidence of primary or metastatic tumor. Apart from CEA, the blood chemistry was within normal limits. Six members of the patient's family have normal CEA levels. A possible explanation for this unique case of marked and persistent elevation of circulating CEA without evidence of cancer is discussed. (Author abstract) (17 Refs) (In FRE)

12. CONCOMITANT HEPATIC RADIATION AND INTRAARTERIAL FLUORINATED PYRIMIDINE THERAPY: CORRELATION OF LIVER SCAN, LIVER FUNCTION TESTS, AND PLASMA CEA WITH TUMOR RESPONSE.

Lokich J, Kinsella T, Perri J, Malcolm A, Clouse M
Dept. Medicine, New England Deaconess Hosp., 185 Pilgrim Road, Boston, MA, 02215
Cancer; 48(12):2569-2574 1981

Sixteen patients with metastatic disease to the liver (12 colorectal and 4 unknown primary tumors) were treated in a pilot study of hepatic irradiation (2,500-3,000 rads in 10-12 fractions) delivered concomitantly with continuous short-term intraarterial infusion of 5-fluorouracil (1 g/d) or FUDR (0.5 mg/kg/d) via a percutaneously placed hepatic artery catheter. Abnormal liver function tests, including SGOT, LDH, and alkaline phosphatase, decreased in all patients by day 7-10 of treatment, and other metabolic factors, including serum cholesterol, calcium, albumin, phosphorous, and uric acid, also decreased, often to subnormal levels by termination of treatment (day 15-20). These chemical alterations did not correlate with tumor response in that the identical pattern was observed in responders (10 patients) as well as nonresponders (6 patients). Objective determinants of response were assessed by serial monitoring of plasma carcinoembryonic antigen (CEA) and liver scan. In 14 patients with elevated CEA levels, tumor response (9 patients), nonresponse (4 patients), and relapse (5 patients) was predicted and confirmed by sequential monitoring of CEA. In one patient, a paradoxical decrease in plasma CEA was associated with progressive disease. The liver scan identified all responding patients but was difficult to quantitate and was delayed for months following subjective clinical response and changes in plasma CEA levels. (Author abstract) (17 Refs)

13. A RETROSPECTIVE STUDY OF SERIAL CEA DETERMINATIONS IN THE EARLY DETECTION OF RECURRENT COLORECTAL CANCER.

Wedell J, Zu Eissen PM, Luu TH, Fiedler R, Van Calker H, Koldowski P, Schlipkoter HW
Kreiskrankenhaus Herford, Schwarzenmoorstr. 70, Postfach 523, 4900 Herford, W. Germany
Dis Colon Rectum; 24(8):618-621 1981

In the past 5 yr, routine CEA determinations have been carried out on all patients after curative operation for colorectal carcinoma. These patients also underwent a clinical follow-up examination in the Oncology Outpatient Department. In 86 patients, recurrence of a tumor was confirmed. In 31 cases, a second-look operation was carried out. The CEA determinations were retrospectively analyzed in these patients and correlated with the time the recurrence of the tumor was diagnosed. These results show that of 86 patients only 15 (17.4%) had pathologic CEA values before clinical symptoms of tumor recurrence. In the patient group with local recurrence, only 11 (23.9%) of 46 patients had previously pathologically raised CEA values. Of 31 patients, 15 (48.4%) underwent curative resection after the second-look operation. At this time, 12 patients (38.7%) still had normal CEA values, whereas only three patients (9.7%) had pathologically raised CEA values. From these results, it was established that early diagnosis of tumor recurrence was very low. Therefore, one should not rely more on postoperative routine CEA determinations in the postoperative monitoring of patients following curative operations for colorectal carcinoma than on regular comprehensive followup examinations of these patients. (Author abstract) (16 Refs)

14. COMPARATIVE STUDY OF NEEDLE BIOPSY AND ALPHA-FETOPROTEIN DETECTION IN THE DIAGNOSIS OF PRIMARY HEPATOCELLULAR CARCINOMA.

Deshpande AD, Patil SD, Talib SH
Dept. Microbiology, Medical Coll. Hosp., Aurangabad, India
J Assoc Physicians India; 29(2):129-132 1981

Efficacy of needle biopsy vs serum alphafetoprotein (AFP) level in the diagnosis of primary hepatocellular carcinoma was examined. Sera from 13 clinically diagnosed patients with hepatocarcinoma (8 histologically verified) were assayed by counter immunoelectrophoresis and agar gel diffusion for AFP levels. One histologically proven case of hepatocellular carcinoma lacked AFP in serum with both methods of detection. One patient with cholangiocarcinoma exhibited AFP in serum, a finding not reported before. Needle biopsy was diagnostically successful in only 6/11 patients with clinically diagnosed hepatocellular carcinoma. (11 Refs)

15. MARKERS IN BREAST CANCER.

Sulitzeanu D

Lautenberg Center General and Tumor Immunology, Hebrew Univ.-Hadassah Medical Sch., POB 1172, 91120 Jerusalem, Israel

Isr J Med Sci; 17(9/10):865-868 1981

A large number of markers associated with breast cancer have been tested for potential usefulness in the initial diagnosis, the evaluation of prognosis, the detection of recurrence and the assessment of response to therapy. Useful but limited information has been obtained in some of the cases by measuring the levels of a number of markers such as carcinoembryonic antigen, ferritin and haptoglobin. None of the known markers are specific for breast cancer and no single marker is elevated in all patients with advanced disease. Studies with multiple markers may provide better coverage. A great deal of attention is being focused on the level of immune complexes that are found in 30 to 50% of the patients. It has been claimed that immune complex levels tend to rise in patients with advanced disease, but these claims await further confirmation. The only markers likely to be useful for early diagnosis are tumor-associated antigens (TAA). Several putative TAA have been identified, but clinical trials employing TAA are still a long way off. Identification of breast cancer TAA may be facilitated by current analyses of immune complexes isolated from patients. Preliminary results of such analyses suggest that immune complexes recovered from patients with breast cancer may contain antigens not present in patients with nonmalignant diseases. (Author abstract) (19 Refs)

16. CEA IN METASTATIC BREAST CANCER (MEETING ABSTRACT).

Siegenthaler P, Mach JP, Vonmoos S

Division of Oncology, Hospital des Cadolles, Epalinges, Switzerland

UICC Conference on Clinical Oncology, October 28-31, 1981, Lausanne, Switzerland. International Union Against Cancer 131 pp., 1981.

The usefulness of carcinoembryonic antigen (CEA) determinations for the follow up of patients with colon cancer is well established. Reports on monitory breast cancer patients are scarce. In an attempt to evaluate the usefulness of the CEA level in breast cancer, 21 patients with metastatic breast cancer have been followed over a period of 3-24 mo (mean 11 mo). Fourteen out of these 21 patients showed an abnormal level ie greater than 5 ng/ml (74%). Among 7 patients with proven metastatic disease and normal CEA levels 3 patients had only minimal metastatic disease in soft tissue whereas 4 patients with extended metastatic lesions in bone and soft tissue repeatedly showed normal CEA levels. Highest CEA values were found with high bulk of disease and with combined metastases in different tissues (visceral and skeletal localization). In most instances there was a rather good correlation between variations of CEA levels with regard to the response or absence of response to the treatment. Thus, repeated determination of CEA in metastatic disease may be of help in monitoring the disease. (no Refs)

17. EVALUATION OF PLEURAL AND ASCITIC FLUID CEA AND HCG LEVELS EXPRESSED AS DIRECT CONCENTRATION AND IN TERMS OF EFFUSION PROTEIN CONCENTRATION FOR DETECTION OF MALIGNANT TUMORS (MEETING ABSTRACT).

Couch WD

Department of Pathology, Baylor University Medical Center, Dallas, TX, 75246

Am J Clin Pathol; 76(3):348 1981

Combining cytology (cytol) with an effusion human chorionic gonadotropin (hCG) and carcinoembryonic antigen (CEA) assay may increase the detection of malignant (mal) tumors associated with pleural (pl) and ascitic (asc) effusions. The following study compares cytol with hCG and CEA assays expressed as concentrations (conc) and effusion total protein conc for tumor detection. CEA (Roche, RIA), hCG (Serono, RIA) and protein (prot) conc (ABA 100) were determined on random pl (n equals 48) and asc (n equals 33) fluids submitted for cytol from 81 patients of whom 55 had mal tumors. Assay levels considered mal were: CEA greater than or equal to 10 ng/ml, hCG greater than or equal to 10 mIU/ml, CEA greater than or equal to 500 ng/g prot, and hCG greater than or equal to 500 mIU/g prot. The following degrees of sensitivity (%) and specificity (%) were obtained for direct conc (ng or mIU/ml): CEA 47 and 88, hCG 36 and 96; CEA and hCG 69 and 88; CEA, hCG and cytol 76 and 88; CEA and cytol 67 and 88; hCG and cytol 55 and 96; cytol alone 40 and 100 and for effusion prot conc (ng or mIU/g prot): CEA 33 and 96, hCG 31 and 96; CEA and hCG 53 and 92, CEA and cytol 64 and 96, hCG and cytol 53 and 96; CEA, hCG and cytol 69 and 92. The results suggest effusion hCG and CEA levels provide a useful adjunct to cytol for the detection of mal tumors. (no Refs)

18. RADIOLABELLED MONOCLONAL ANTI-CEA ANTIBODIES FOR SCANNING DETECTION OF HUMAN CARCINOMAS (MEETING ABSTRACT).

Mach JP, Buchegger F, Forni M, Ritschard J, Accolla R, Carrel S

Ludwig Institute for Cancer Research, Lausanne Branch, 1066 Epalinges, Switzerland

UICC Conference on Clinical Oncology, October 28-31, 1981, Lausanne, Switzerland. International Union Against Cancer 131 pp., 1981.

Monoclonal antibodies with a high specificity and affinity for carcinoembryonic antigen (CEA) were purified from hybridoma ascites, labeled with 131I and injected first in nude mice bearing human carcinoma grafts and later in tumor bearing patients. The results from the pilot human studies, obtained by external scanning of the patients and by direct measurement of the radioactivity in resected tumors and adjacent normal tissues showed that monoclonal anti-CEA antibodies are capable of specific tumor localization in some patients. Ten out of 20 patients with colon or pancreas carcinoma injected with labeled monoclonal antibodies showed positive 'immuno-scintigraphy'. The specificity indices of localization obtained by comparing in fragments of tumor and normal tissues, the 131I radioactivity of the antibodies with the 125I radioactivity of control normal mouse IgG injected simultaneously with the antibodies, gave values ranging from 2-6. The non-specific accumulation of antibody radioactivity in the reticuloendothelium was much lower than with polyclonal antibodies. These encouraging results, however, are not sufficient to recommend this method of 'immune-scintigraphy' for routine tumor detection. (1 Ref)

19. THE LEUCOCYTE ADHERENCE INHIBITION TEST (LAI) AND CARCINOEMBRYONIC ANTIGEN (CEA) IN THE DIAGNOSIS AND FOLLOW UP OF PATIENTS WITH COLORECTAL CARCINOMA (MEETING ABSTRACT).

Shani A, Weissman Z, Cohen Z, Bentwich Z
Unit of Oncology and Department of Medicine, Kaplan Hospital, Rehovot, Israel
UICC Conference on Clinical Oncology, October 28-31, 1981, Lausanne, Switzerland. International Union Against Cancer 131 pp., 1981.

Two tumor markers, LAI and CEA, were studied for their value in diagnosis and follow-up of patients with colorectal carcinoma. Fifty-seven blood samples from patients with proven colorectal carcinoma at various stages of diseases and 42 controls were studied. Samples were taken preoperatively and every 4 mo thereafter. Results show that the LAI test was positive in 31/54 (57.4%) of preoperative colorectal carcinoma patients, while only 4/42 (9.5%) of the control group were positive. The CEA test identified 23/57 (40.3%), whereas combining the two tests LAI and CEA together, 38/54 (70.3%) of the patients were correctly diagnosed. An inverse relation was found, however, between the two: 16/28 (57%) of LAI positive patients had a negative CEA and 7/23 (30.4%) of LAI negative patients had positive CEA. Sequential LAI studies revealed that 18/31 (58.0%) of the patients with positive LAI changed postoperatively to negative, with no evidence of disease in 16. Of the 23 preoperative negative LAI, 20 stayed negative after the operation. These data imply that the pair of test LAI and CEA are promising in the diagnosis of colorectal carcinoma. The combination of LAI and CEA may thus serve for further immune staging of patients with colorectal carcinoma. (no Refs)

20. COLORECTAL CARCINOMA. PROPOSALS OF THE ULM TUMOR CENTER.

Betzler M
Chirurgische Klinik der Universitat, Im Neuenheimer Feld 11, D-6900 Heidelberg, W. Germany
MMW; 123(44):1657 1981

Follow-up procedures for patients treated surgically for colorectal carcinoma are presented. The basic follow-up program includes physical examination and determination of the carcinoembryonic antigen (CEA) level at 2-mo intervals during the 1st yr, at 3-mo intervals during the 2nd yr, and at 6-mo intervals during the 3rd and 4th yr. An occult blood test is performed at mo 6, 12, 18, 36, and 48, chest x-ray at 12-mo intervals, colon contrast examination at mo 12 and 48. Rectosigmoidoscopy is performed at mo 2, 6 and 24 in patients subjected to anterior resection. (no Refs) (In GER)

21. GASTRIC CANCER. PROPOSAL OF THE ULM TUMOR CENTER.

Betzler M
Chirurgische Klinik der Universitat, Im Neuenheimer Feld 110, D-6900 Heidelberg, W. Germany
MMW; 123(44):1647 1981

A timetable for the follow-up of gastric cancer patients after radical surgery is proposed. Physical examination and laboratory tests, including the determination of carcinoembryonic antigen, are performed at 2-mo intervals during the 1st yr, at 3-mo intervals during the 2nd yr, and at 6-mo intervals during the 3rd and 4th yr. Endoscopy is performed at mo 2, 6, 10, 15, 24 and 48. Sonography is carried out at mo 6, 12, 18, 24, 36 and 48. (no Refs) (In GER)

22. BREAST CARCINOMA. PROPOSAL OF THE ULM TUMOR CENTER.

Betzler M
Chirurgische Klinik der Universitat, Im Neuenheimer Feld 110, D-6900 Heidelberg, W. Germany
MMW; 123(44):1644 1981

A proposal concerning the follow-up of breast cancer patients is presented. Two hundred eighty-seven breast cancer patients were followed for 5 yr. Locoregional recurrences and/or metastases were found in 5.6% of the patients, distant metastases in 11.2%. Mastectomy for contralateral carcinoma was indicated in six cases (2.1%). Symptoms were produced by 10/12 bone metastases. Breast cancer patients were submitted to physical examinations and certain enzymes and carcinoembryonic antigen levels were determined at 3-mo intervals during the first 2 yr, then at 6-mo intervals. Mammography, chest x-ray, and gynecological examinations are performed annually. The family doctor is the link between the patient and the clinic during the follow-up. (no Refs) (In GER)

23. BRONCHIAL CARCINOMA. PROPOSAL OF THE RUHRLAND CLINIC, ESSEN.

Maassen W
Ruhrlandklinik, Tuschener Weg 40, D-4300 Essen 16, W. Germany
MMW; 123(44):1656 1981

A follow-up program for patients with bronchial carcinoma is proposed. The general status of the patient should be evaluated at 6-mo intervals during the first 3 yr after surgery along with chest x-ray in two planes, assessment of the lymph node status, and the determination of laboratory parameters. The value of the determination of the carcinoembryonic antigen level has not yet been clearly established. (no Refs) (In GER)

24. CLUES TO CANCER OF THE DIGESTIVE SYSTEM.

Segal HL
Genesee Hosp., Rochester, NY
Consultant; 21(12):101-103 1981

Four noninvasive tests are described which may suggest presence of malignancy or indicate the need for further study: the tubeless test for gastric secretory activity; the fecal occult blood test; tests for immune system-associated substances (carcinoembryonic antigen, alpha-fetoprotein), and tests of mineral metabolism (hypercalcemia, copper/zinc ratio). (7 Refs)

ULTRASTRUCTURE/ CYTOCHEMISTRY

25. TISSUE LOCALIZATION OF CARCINOFETAL PROTEINS (CEA, AFP, HCG) IN CERVICAL CANCER AND OVARIAN TUMOR, UTILIZING IMMUNOHISTOCHEMICAL TECHNIQUE EMPLOYING ENZYME-COUPLES ANTIGEN ANTIBODY REACTION (MEETING ABSTRACT).

Kodama S, Obata N, Hando T, Sato Y, Takeuchi S
Department of Obstetrics and Gynaecology, Niigata University School of Medicine, Niigata, Japan
Obstetrics and Gynaecology: 8th Asian Congress, October 25-31, 1981, Melbourne, Australia. Asia and Oceania Federation of Obstetricians and Gynaecologists 352 pp., 1981.

Immunoperoxidase staining (PAP method) for carcinoembryonic antigen (CEA), alpha fetoprotein (AFP) and human chorionic gonadotropin (HCG) was performed for 91 patients with carcinoma of the cervix and 65 patients with ovarian tumor. Cervical cancer consisted of 10 carcinoma in situ (CIS), 71 invasive squamous cell carcinoma, and 10 adenocarcinoma. Ovarian tumor was examined in 20 serious tumors (5 benign, 4 low grade malignancy, and 9 malignant cases), 21 mucinous tumors (3 benign, 4 low grade malignancy, and 9 malignant cases), 4 endometroid adenocarcinoma, 6 mesonephroid adenocarcinoma, 10 embryonal carcinoma, and 5 solid teratoma. A) CEA: CEA was present in 20.0% of CIS, in 59.2% of invasive squamous cell carcinoma and in 70.0% of adenocarcinoma of the cervix. In cervical cancer, CEA was common in large cell nonkeratinizing squamous cell carcinoma and less commonly in small cell carcinoma but there was no relationship between tissue localization and differentiation in adenocarcinoma. In ovarian tumor, CEA was present in 50% of benign, in 100% of low grade malignancy and in 100% of malignant mucinous cystadenocarcinoma. Fifty percent of mesonephroid and 80% of solid teratoma also had been localized in their tissue. Nine patients with elevated initial plasma CEA level and 19 of 32 with normal plasma level were positive for CEA in cervical cancer. In ovarian tumor, all cases of negative tissue-localization and 63% of positive tissue were within normal plasma level. B) AFP: AFP was detected in 80% of solid teratoma and 90% of embryonal carcinoma. All solid teratoma and 78% of embryonal carcinoma had elevated initial plasma level. C) HCG: HCG in ovarian tumor will be mentioned. (no Refs)

26. A COMPARISON OF GAMMA GLUTAMYL TRANSPEPTIDASE ACTIVITY IN BENIGN HUMAN MAMMARY LESIONS AND PRIMARY, RECURRENT AND METASTATIC BREAST CARCINOMA (MEETING ABSTRACT).

Levine SE, McCarty KS, McCarty KS, Michalopoulos GK

Departments of Pathology. Duke University Medical Center, Durham, NC, 27710

Am J Clin Pathol; 76(3):354 1981

Gamma glutamyl transpeptidase (GGT) has been suggested to respresent an 'oncofetal marker' in liver and skin neoplasia. This enzyme is histochemically demonstrable in human breast eipthelium. A characteristic pattern of luminal and apical GGT activity greater than non-apical (homogeneous) cytoplasmic staining is seen in benign breast tissue (23 benign and dysplastic breast lesions). Malignant breast tumors (91 primary and 17 metastatic) exhibit a bimodal distribution of GGT staining intensity ranging from markedly increased to absent cytoplasmic staining. Metastatic breast tumors exhibited a GGT activity curve skewed toward high GGT scores when compared to the bimodal GGT activity curve for primary tumors. Although the GGT activity of the tumors was independent of estrogen-progesterone receptor content, the GGT activity of a tumor appears to complement the tumor's estrogen and progesterone receptor content as a prognostic indicator of tumor behavior. Shifts in GGT staining from the characteristic benign pattern to weak or intense homogeneous cytoplasmic histochemical activity are observed in 'pre-malignant' or 'borderline' lesions. (no Refs)

27. AN ULTRASTRUCTURAL STUDY OF OVARIAN YOLK SAC TUMOR - AN INVESTIGATION OF ITS HISTOGENESIS COMPARED TO THAT OF HUMAN YOLK SAC (MEETING ABSTRACT).

Takashina T, Kawase N, Hashimoto M

Department of Obstetrics and Gynaecology, Sapporo Medical College, Sapporo, Japan

Obstetrics and Gynaecology: 8th Asian Congress, October 25-31, 1981, Melbourne, Australia. Asia and Oceania Federation of Obstetricians and Gynaecologists 352 pp., 1981.

In the present study for the purpose of investigating the histogenesis of yolk sac tumor, 7 cases of tumor and 9 cases of human yolk sac were used. Histological and ultrastructural investigation together with the immunofluorescent antibody technique revealed the following results. Ultrastructurally yolk sac endodermal cell prior to the 7th wk of pregnancy proved to have microvilli, abundant glycogen forming rosettes, rough endoplasmic reticulum (rER), mitochondria coupled with rER and ovoid electron-dense amorphous granules which were found microscopically to be diastase-resistant and to have a PAS-reaction positive. Morphologically endoderm of the 8th wk of pregnancy showed degenerative changes. Ultrastructural similarity between the tumor and human yolk sac seems to resemble the yolk sac endoderm before the 7th wk of pregnancy. The tumor cells which form the epithelial mantles of the Schiller-Duval bodies closely resemble the endodermal cells facing the yolk sac cavity in that abundant glycogen granules, rER, mitochondria, short irregular microvilli on the cell surface and remarkable nucleoli with thread-like nucleolonema are seen. Both the tumor cells facing the pericyte and the tumor cells which form the endodermal sinus structures and clear-cell entoblastic patterns resemble the endodermal cells facing the mesenchyme in views of the finding of intracellular organelles, the presence of basement membrane-like material outside the cytoplasm and a tubular structure. Immunofluorescent findings suggest that the tumors have an ability to synthesize alpha fetoprotein. (no Refs)

REVIEWS/ OTHER RELATED STUDIES

28. STUDIES ON PLACENTAL ANEMIA-INDUCING FACTOR. REPORT IV. IMMUNOLOGICAL AND BIOLOGICAL INVESTIGATION OF HUMAN PLACENTAL ANEMIA-INDUCING FACTOR.

Inoue S

Second Dept. Surgery, Hirosaki Univ. Sch. Medicine, Hirosaki, Japan

Hirosaki Igaku; 33(1):23-36 1981

Human placental anemia-inducing factor (PAIF), purified from the anemia-inducing fraction (P-62) of human placentas, had a specific precipitin line in the region of IgA and/or IgM when analyzed by immunoelectrophoresis. With the aid of Ouchterlony's gel-diffusion method, PAIF was shown to have antigenicity common to P-62, DEAE-Fr1 (a fraction of P-62 purified with the aid of Narita's method), and CL-62 (mucoprotein fraction from metastatic liver tumors), while the antigenicity of the PAIF was not common to that of NL-62 (noncancerous liver antigen). The PAIF was thought to have potential application as a cancer associated antigen similar to alpha-fetoprotein and carcinoembryonic antigen. (20 Refs) (In JPN)

29. CONTRACEPTIVES AND THE LIVER.

Schmid M
Medizinische Klinik, Stadtspital Waid, Tiechestr. 99, CH-8037 Zurich, Switzerland
Leber Magen Darm; 11(5):216-226 1981

Studies on the relationships between the use of oral contraceptives (OC) and hepatic diseases are reviewed. The relationship between the long-term use of OC and benign hepatocellular adenoma is now beyond doubt. The progestagen component of the ovulation inhibitor acts as an enzyme inducer which may facilitate the formation of carcinogenic metabolites from various substances, and prompt elimination of these metabolites with the bile is prevented by the cholestatic effect of the estrogens. The relationship between OC and focal nodular hyperplasia is less evident. Here, the congenital hamartomatosis represents a site of least resistance for the hormones, but the steroid hormones are probably responsible for the vascular complications, especially for peliosis. Malignant hepatic tumors (hepatocellular carcinoma and especially hepatoblastoma and angiosarcoma) in connection with the long-term use of OC are extremely rare. The alpha-fetoprotein level is usually not increased significantly in patients with hepatocellular adenoma and carcinoma due to OC. (52 Refs) (In GER)

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STRUCTURE/ IDENTIFICATION/ CHARACTERIZATION

1. IMMUNOLOGICAL DELINEATION IN NORMAL AND MALIGNANT CELLS OF A MEMBRANE PROTEIN INVOLVED IN GLUCOSE TRANSPORT. I. PREPARATION AND PROPERTIES OF THE ANTIBODY.

Gingrich RD, Wouters M, Bramwell ME, Harris H
Sir William Dunn Sch. Pathology, South Parks Road, Oxford OX1 3RE, England
J Cell Sci; 52:99-120 1981

Partially purified preparations of the 200,000 Mr membrane glycoprotein described by Bramwell and Harris were used as antigens to generate monoclonal antibodies. Whether the protein was prepared from human or mouse tumors, the mice immunized with it yielded monoclonal antibodies of broadly similar specificities. All the antibodies obtained were of the immunoglobulin M class, despite a prolonged immunization schedule, and recognized an antigen that was present on the surface of mouse, rat and human cells. One such antibody, M/27, was studied in detail. With the exception of two rat kidney cell lines, the antigen detected by M/27 was found on the surface

HE 20.3173/2

of all cells grown in culture, whether malignant or not. However, in the mouse, the species in which the antibody was generated, M/27 discriminated sharply between malignant tumors and normal tissues excised directly from the animal. In normal adult or embryonic mouse tissues, whether they were composed of multiplying cells or not, the antigen detected by M/27 was present on the cell surface only at the lower limit of detection, if at all. Malignant mouse tumors grown in the animal produced large amounts of the antigen. Explantation of embryonic mouse fibroblasts induced the expression of the antigen, which was not detected on these same cells in their normal habitat in the growing embryo. Conversely, non-malignant cells that express the antigen in vitro cease to do so when they are re-introduced into the animal. The antigenic determinant appeared to be polypeptide in nature rather than polysaccharide. (Author abstract) (40 Refs)

2. HYBRIDOMA MONOCLONAL ANTIBODY: USE IN DEFINING SURFACE ANTIGENS ON HUMAN LUNG CARCINOMA CELLS.

Kasai M, Saxton RE, Holmes EC, Burk MW, Morton DL, Bonnard, Alexander P, Ferrone S, Ivanyi P, Nathanson SD, Pious D, Embleton MJ
54-140 CHS, UCLA Sch. Medicine, Los Angeles, CA, 90024
Transplant Proc; 13(4):1942-1946 1981

Surface antigens on UCLA-SO-P3, the squamous cell lung carcinoma cell line derived from a 53-yr-old man, were compared with those on PL3, the autologous lymphoblast line obtained from the same patient. Using the autologous cell lines, two hybridomas were selected which secrete monoclonal antibodies that bind antigenic determinants present at high density on the carcinoma cells but not on the paired lymphoblastoid cells. The two cloned hybridomas, designated 169D4 and 169F3, were grown as ascites tumors in mineral oil-primed BALB/c mice. The two binding curves obtained by titration of hybridoma cells with P3 and PL3 target cells were compared. An end-point titer greater than 1:100,000 for both antibodies to the P3 carcinoma but only 1/:10 to PL3 for the 169D4 monoclonal antibody and 1:100 for 169F3 was revealed. The shapes of these antibody binding curves showed that the antigenic determinants recognized by the two monoclonal antibodies were present at high density on the P3 carcinoma but at low density or absent from the PL3. The immunoglobulin isotype of both 169D4 and 169F3 monoclonal antibodies was identified as IgM. The two monoclonal antibodies were tested for binding to 12 carcinoma cell lines, 9 melanoma, 2 sarcoma, 4 lymphoblast, and 1 human embryonic cell line. Among the cell lines tested, only the lung carcinoma P3 and the colon carcinoma HT29 expressed detectable levels of 169D4 surface antigen. 169F3 monoclonal antibody recognized an epitope present on every human tumor cell line and on human embryo cells, but not on the lymphoblastoid cell lines. (6 Refs)

3. BCA (BREAST CANCER ANTIGEN). PRELIMINARY BIOCHEMICAL AND IMMUNOCHEMICAL STUDIES (MEETING ABSTRACT).

Accinni R, Bailo M, Cavalca V, Botta M, Bartorelli A
Univ. of Milano, Milan, Italy
UICC Conference on Clinical Oncology, October 28-31, 1981, Lausanne, Switzerland. International Union Against Cancer 131 pp., 1981.

In previous investigations we pointed out a carcinoembryonic antigen (CEA)-like antigen in a breast cancer pool, otherwise absent from control normal breast tissue. After demonstrating its different distribution in 48 primary breast carcinomas, we exploited a carcinoma pool, with high antigenic content, to extract BCA by means of 3M KCl. Subsequently, the antigen was purified by concanavalin A-Sepharose and bioabsorption chromatography, and labelled with Na 125I to be employed as tumor marker in the radioimmunoassay (RIA). Its physico-chemical and immunological characteristics, especially compared with those already well known for CEA, were analyzed. Preliminary High Performance Liquid Chromatography (HPLC) studies, on TSK 3000 and TSK 4000 columns (Trade Mark of Toyosoda), showed substantial differences in the retention times, therefore in the hydrodynamic vol, pointing out a complex stereochemical structure both for BCA and CEA. Differences in the isoelectric points were detected for these acidic glycoproteins by isoelectric focusing. Agar immunodiffusion, RIA and immunoperoxidase investigations showed interesting analogies and substantial differences for these two tumor markers. Besides, by applying on TSK 4000 columns CEA-positive sera, employed as experimental model, we observed that the antigen is eluted with the same retention time as the antigen extracted and purified from liver metastases. (no Refs)

4. CEA AND NCA ARE PROBABLY BIG ALPHA 1-ACID GLYCOPROTEIN (MEETING ABSTRACT).

Miyazaki T, Ijichi H, Kajita Y, Fujiyama Y, Ochi Y, Hosoda S, Hachiya T
2nd Department of Internal Medicine, Kyoto Prefect University of Medicine, Kyoto, Japan
Proceedings of the Japanese Cancer Association, 40th Annual Meeting, October 1981, Sapporo, Japan. The Association 415 pp., 1981.

The perchloric acid extract from cancerous tissue was fractionated on Sephadex G-200, and the first eluted fraction (enriched carcinoembryonic antigen (CEA)) was subjected to anti-AG bound to Sepharose. The bound fraction to the column was labeled with 125I, and then applied to Sephadex G-200 with carrier protein. The eluted radioactivity (RA) was found mainly in the large molecular fraction (Fr 1) and a small amount was found in the smaller molecular fraction (Fr 2). The RA of Fr 1 reacted with either AG antibody or CEA antibody, but the RA of Fr2 reacted only with AG antibody. The fact supports tha t CEA may be big AG. A similar experiment non specific cross-reacting antigen (NCA) also showed immunoreactivity with AG antibody. (no Refs)

ASSAY PROCEDURES/ SYNTHESIS

5. SIMULTANEOUS ENZYME IMMUNOASSAY OF CARCINOEMBRYONIC ANTIGEN IN PLEURAL EFFUSION AND SERUM.

Asseo PP, Tracopoulos GD
(c/o Tracopoulos) 10th Medical Unit, Athens Chest Hosp. 'Sotiria', Messogeion 152, Athens, Greece
Am J Clin Pathol; 77(1):66-71 1982

A carcinoembryonic antigen (CEA) enzyme immunoassay test was used to estimate its value in the differential diagnosis of malignant and non-malignant pleural effusions. Paired pleural fluid and serum CEA determinations were performed in 107 patients, 53 with malignant and 54 with non-malignant pleural disease. CEA values uniformly lower than a cut-off level of 5.0 ng/ml were found in the pleural fluid and the serum in the non-malignant group, whereas in the malignant group, values higher than the cut-off level were present in the pleural fluid in 37 (69.8%), and in the serum in 30 (56.6%) of the examined patients. All 30 patients with elevated serum CEA levels also had pleural fluid CEA above 5.0 ng/ml. The results of this study demonstrate that although pleural fluid CEA values below 5.0 ng/ml do not exclude malignancy, increased values strongly suggest that the fluid is of malignant origin. Pleural fluid CEA determination had a 13.2% higher sensitivity, compared with that of the serum, in detecting malignant pleural involvement, yet with no statistical significance. (Author abstract) (27 Refs)

6. IN VITRO SYNTHESIS OF ALPHA-FETOPROTEIN AND HUMAN CHORIONIC GONADOTROPIN IN TESTICULAR CANCER.

Javadpour N, Soares T, Princler GL
Surgery Branch, NCI, Bethesda, MD, 20205
Cancer; 49(2):303-307 1982

In vitro synthesis of alpha-fetoprotein (AFP) and human chorionic gonadotropin (HCG) utilizing 14C-L-leucine and 14C-L-lysine incorporation in fresh testicular cancer tissue of five patients was demonstrated. Radioimmunoassay, immunoprecipitation of 14C-HCG and 14C-AFP, and quantitation of AFP and HCG. This in vitro synthesis of AFP and HCG was correlated with immunocytochemical staining in the cancer cells of the five patients. (Author abstract) (8 Refs)

7. QUANTITATIVE STUDY OF CEA BY MEANS OF RADIOIMMUNOASSAY OF EXTRACTS OF BENIGN AND MALIGNANT TUMORAL TISSUES OF THE FEMALE GENITAL APPARATUS.

Pandolfo J, Aguirre B, Robles A, Jaumandreu CA, Touya E
Clinica Ginecotocologica A, Facultad de Medicina, Montevideo, Uruguay
Rev Biol Med Nucl; 13(1/2):21-23 1981

Quantitative determination of carcinoembryonic antigen (CEA) was studied by means of radioimmunoassay (RIA) on seven tissue extracts of five patients with inflamed ulcerated ectropion, uterine myomatosis, endocervical polyp with myomatosis and right ovarian cyst, uterine myomatosis with ovarian cy stic adenofibroma (UMOCAF), and uterine neck cancer (UNC) Grade IV treated with radiotherapy. The CEA contents of the uterine necks in the five patients ranged from 4.1 to 39.4 nanograms (ng)/g fresh tissue. In the case of UMOCAF, the ovarian CEA content was 22.8 ng/g. The CEA content of the lymph node of the UNC patient was 11.9 ng/g. Although the range of CEA values for normal women was not satisfactorily established, the CEA values in different pathological processes were found to be altered, probably due to changes in local cellular metabolism. (26 Refs) (In SPA)

EXPERIMENTS IN ANIMAL SYSTEMS

8. ULTRASTRUCTURE AND IMMUNOHISTOCHEMICAL STAINING OF A TRANSPLANTED ENDODERMAL SINUS TUMOR.

Suganuma T, Takao S, Suzuki S, Tsuyama S, Nishi M, Murata F
(c/o Murata) Dept. Anatomy, Kogoshima Univ. Sch. Medicine, Kogoshima 890, Japan
Virchows Arch [Cell Pathol]; 38(2):177-187 1981

An endodermal sinus (yolk sac) tumor was successfully transplanted into athymic nude mice. Histologic and ultrastructural investigations revealed that the transplanted tumor had a characteristic appearance with numerous Shiller-Duval bodies, endodermal sinus structures and ultrastructural profiles as previously described in human material. The endodermal sinus tumor and normal human yolk sac have been found to synthesize not only alpha-fetoprotein (AFP), but also other serum proteins, namely, albumin, prealbumin, alpha1-antitrypsin, and transferrin. Serological study by radioimmunoassay demonstrated AFP, carcinoembryonic antigen (CEA) and human chorionic gonadotropin (HCG) in the sera of the tumor-bearing nude mice and in cyst fluid from the transplanted tumor. Immunohistochemical investigation using the unlabeled antibody peroxidase-antiperoxidase method showed that the tumor cells produced CEA, alpha1-antitrypsin, transferrin, HCG as well as AFP. These immunohistochemical staining properties were correlated with the findings on radioimmunoassay. (Author abstract) (28 Refs)

9. MODIFICATION OF ALPHA-FETOPROTEIN AND ALBUMIN SYNTHESIS BY DIMETHYLSULFOXIDE IN AN ESTABLISHED LINE OF MOUSE HEPATOMA CELLS.

Higgins PJ
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Cell Struct Funct; 6(3):295-300 1981

The effect of dimethylsulfoxide (DMSO) on synthesis of albumin (ALB) and alpha-fetoprotein (AFP) was studied in mouse epithelioid tumor cells of line BW1, derived from transplantable BW7756 mouse hepatoma. BW1 cultures were exposed to DMSO (final concentration 0, 0.5, 1.0, or 3.0%) for 4 days. ALB and AFP in cell lysates and culture supernatants were quantified using specific rabbit antisera. AFP and ALB accounted for 0.51 and 0.53%, respectively, of total cell-associated protein (TCAP) in BW1 cultures not treated with DMSO. Intracellular (IC) and extracellular (EC) ALB and AFP were increased by exposure of cells to DMSO. The ALB percentage of TCAP increased with increasing concentrations of DMSO. Max AFP percentage of TCAP was produced by 0.5% DMSO; above this level the AFP fraction declined slightly, although in all DMSO treated cultures the AFP fraction was approx 60% greater than in control cultures. Treatment with 1% DMSO increased EC AFP by 156% and EC ALB by 214%. Increases in IC AFP and ALB evidently were not due to inhibition of transport mechanisms. Apparently ALB synthesis is dependent on DMSO concentration, while AFP synthesis, once initiated, is independent of DMSO concentration. DMSO treatment reduced the final number of cells in culture by 57% with 1% soln and by 84% with 3% soln. Results indicate that in vitro expression of growth properties correlates with an enhanced capacity for production of differentiated gene products. (15 Refs)

10. IMMUNOCYTOCHEMICAL DEMONSTRATION OF ALPHA-FETOPROTEIN UPTAKE BY PRIMARY CULTURES OF FETAL HEMISPHERE CELLS FROM MOUSE BRAIN.

Uriel J, Faivre-Bauman A, Trojan J, Foiret D
Institut de Recherches Scientifiques sur le Cancer, B.P. No. 8, 94802 Villejuif, France
Neuosci Lett; 27(2):171-175 1981

Brain primary cultures initiated from fetal albino Swiss mice and grown in serum-free medium (SFM) were incubated for 24 hr in the presence of 1 ml SFM containing 80-150 ug of mouse alpha-fetoprotein (AFP). An indirect immunoperoxidase technique, with appropriate controls, was used to localize mouse AFP. Peroxidase activity was developed by incubation in diaminobenzidine. The number of AFP-positive cells and the intensity of staining (phase microscopy) increased with maturation up to days 8 and 9. No AFP-labeling was observed when, prior to incubation, antibodies to AFP were treated with an AFP-immunoadsorbent polymer of mouse amniotic fluid. The results support the hypothesis that the intracellular presence of AFP in the developing nervous systems of mammals and birds is mostly if not entirely due to protein uptake rather than synthesis. (13 Refs)

11. DYNAMICS OF SERUM ALPHA-FETOPROTEIN DURING SPONTANEOUS HEPATOCELLULAR CARCINOMA DEVELOPMENT IN MICE.

Princler GL, Vlahakis G, Kortright KH, Okada S, McIntire KR
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Eur J Cancer Clin Oncol; 17(12):1241-1248 1981

C3H-AvyfB mice have been studied over their normal life span and 69% developed hepatocellular carcinoma (HCC). Forty-seven mice were bled at monthly intervals, and individual serum alpha-fetoprotein (AFP) profiles are presented for 36 animals. Most of these profiles are quite irregular. Sixty percent of the 15 male mice had a transient serum AFP elevation at 5 mo, reaching a mean of 289 ng/ml, compa red to a mean of 208 ng/ml for those male mice without a transient AFP elevation and a mean of 185 ng/ml in male mice at 2-4 mo of age. All of these male mice and others were tested for murine hepatitis virus and found to be negative. Mice with this early AFP peak tended to have a lower incidence of HCC and much lower AFP values later in life than those not having an early peak, but this difference was not statistically significant. Of the mice whose serum AFP concentration exceeded 300 ng/ml beyond 6 mo of age, 23% (9/39) experienced a subsequent pronounced decline in AFP, averaging 74% of previous peak values for males and 44% for females. Of the 39 mice evaluated, 35 were autopsied and 50% (4/8) of these 'serum AFP regressors' had microscopic evidence of lymphocytic infiltration in their livers, as compared to 15% (4/27) of the 'nonregressors' that had a similar change. (Author abstract) (15 Refs)

12. SYNTHESIS OF ALPHA-FETOPROTEIN (AFP) AND CELL PROLIFERATION IN REGENERATING LIVERS OF NMRI MICE AFTER PARTIAL HEPATECTOMY: AN IMMUNOHISTOCHEMICAL AND AUTORADIOGRAPHIC STUDY WITH 3H-THYMIDINE.

Tuczek HV, Fritz P, Wagner T, Braun U, Grau A, Wegner G
Dept. Clinical and Experimental Pathology, Robert-Bosch-Hosp., Auerbachstrasse 110, D-7000 Stuttgart 50, W. Germany
Virchows Arch [Cell Pathol]; 38(2):229-237 1981

To get more information concerning the relation between cell proliferation and the synthesis of alpha-fetoprotein (AFP), liver regeneration and AFP production was followed simultaneously in short intervals in NMRI mice after two-thirds hepatectomy using autoradiographic and immunohistochemical methods. The results indicate that AFP synthesis is not linked closely to cell proliferation in the sense that each proliferating hepatocyte synthesizes AFP during a definite phase of the cell cycle. However, AFP production, as measured by the index of anti-AFP positive hepatocytes, occurs in a very small population of parenchymal cells when the bulk of the hepatocytes has just passed the S-phase and is considered to be in the G2-, M or early G1-phase of the cell cycle when the cells are still in an undifferentiated state. (Author abstract) (58 Refs)

13. EFFECT OF HUMAN LEUKOCYTE INTERFERON ON YOLK SAC TUMOR TRANSPLANTED IN NUDE MICE (MEETING ABSTRACT).

Sawada M, Hayakawa K, Matsui Y, Nishiura H, Okudaira Y, Kishida T, Kurokawa K

Department of Gynecology, Osaka University, Osaka, Japan

Proceedings of the Japanese Cancer Association, 40th Annual Meeting, October 1981, Sapporo, Japan. The Association 415 pp., 1981.

Human yolk sac tumor of the ovary transplanted in BALB/C nude mice designated as YST-2 was used in this experiment. YST-2 tumor cells preserve the characteristics of a human yolk sac tumor of the ovary, and were capable of producing alpha-fetoprotein (AFP). Four x 10 IU of human WBC interfer on (HLIF) was administered ip to tumor-bearing nude mice everyday for eight days. Evaluation of response was made by examining tumor size, relative tumor size, serum AFP level of mice, tumor/control % (T/C) and histologic appearance. Optimal relative tumor size of treated tumor was 0.76 while that of the control tumor was 4.0. T/C% at the end of the experiment was 90.1. The level of AFP showed good correlation with the size of tumor. Histologic changes were recognized in treated tumor. HLIF was active in regressing of human yolk sac tumor. (no Refs)

14. RADIOLABELING OF MONOCLONAL ANTITUMOR ANTIBODIES: COMPARISON OF I-125 AND IN-111-ANTI-CEA WITH GA-67 IN A NUDE MOUSE-HUMAN COLON TUMOR MODEL (MEETING ABSTRACT).

Halpern SE, Stern PL, Hagan PL, Chen A, David GS, Desmond WJ, Adams TH, Bartholomew RM, Frincke JM, Brautigam CE

University of California, Veterans Administration Medical Center, San Diego, CA

Clin Nucl Med; 6(9S):453 1981

Monoclonal antitumor antibodies (MoAbs) labeled with I-131 have been shown to concentrate in murine tumors. Work in our own laboratory indicates that I-125-anti-carcinoembryonic antigen (CEA) MoAbs, while stable in vitro, dehalogenate in vivo. The purpose of the following study was to compare I-125 and In-111-anti-CEA MoAbs with Ga-67 in a nude mouse-human colon tumor model. Anti-CEA was labeled with I-125 using the Bolton-Hunter method, shown to be stable in saline at 37 C over a 72-hr period and to react with specific antigen to 70-80% efficiency. The antibody was conjugated with diethylenetriamine pentaacetic acid (DTPA) using DTPA anhydride, then labeled with In-111. The In-111-anti-CEA complex was stable in vitro with greater than 70% binding to CEA. Nude mice bearing human colon tumors were injected with similar quantities of both isotopes and sacrificed at 4, 24, 48 and 72 hr. Distribution and excretion studies were performed. Tissue concentrations were computed as % injected dose/gm (%ID/G). Peak tumor %ID/G occurred for I-125 (5%) at 4 hr, for In-111 (23%) at 72 hr, and for Ga-67 (5%) at 24 hr. Greater than 70% of the I-125 was excreted in the urine by 48 hr, compared to less than 10% of the In-111. Tumor/blood and muscle ratios for In-111-anti-CEA were 8:1 and 39:1 at 72 hr. In-111-anti-CEA MoAbs are superior to iodinated anti-CEA MoAb or Ga-67 as a potential tumor imaging agent and should be used preferentially if imaging studies are undertaken with radiolabelled MoAbs in humans. (no Refs)

IMMUNOLOGIC INTERACTIONS

15. COLORECTAL CARCINOMA: EVIDENCE FOR CIRCULATING CEA-ANTI-CEA COMPLEXES (MEETING ABSTRACT).

Mavligit G, Stuckey S
University of Texas System Cancer Center, M.D. Anderson Hospital and, Tumor Institute Houston, TX
UICC Conference on Clinical Oncology, October 28-31, 1981, Lausanne, Switzerland. International Union Against Cancer 131 pp., 1981.

Despite the increasing usefulness of serial plasma CEA (carcinoembryonic antigen) determination in monitoring patients with subclinical colorectal cancer, a rising CEA as measured by the conventional radioimmunassay can only be expected in approx 70% of clinically documented cases with recurrent disease. Lack of CEA production by, or release from the growing tumor, and,' perhaps a modification in its antigenic moiety rendering it nonassayable were all advocated as tentative explanations. Recent studies by Staab, et al, provided strong evidence in support of the presence of circulating CEA-anti-CEA complexes. We surmised that a presplitting of such putative CEA-anti-CEA complexes in a given plasma sample must result in a higher measurable CEA. Furthermore, the eluted anti-CEA from the splitting procedure must rebind purified CEA. Plasma samples were eluted with 2.5 M MgCl2 and the IgG component was then precipitated out by Protein A. Significant increments in measurable CEA were effected in 11 of 15 patients with disseminated colorectal cancer and in five of ten patients with the Duke's C category. Complex-released IgG from a patients with a higher MgCl(2)-induced CEA increment effected a greater specific binding of I125-CEA than a similar IgG eluate from a patient with a negligible CEA increment. Our data suggest that CEA is autoimmunogenic and may result in circulating CEA-anti-CEA complex formation. (no Refs)

16. MEDIASTINAL GERMINOMA: ASSOCIATION WITH HUMORAL ANTIBODIES AGAINST SPERMATOPOIETIC CELLS (MEETING ABSTRACT).

Gasser AB, Zeltner T, Brunner K, Hess MW
University of Bern, 3010 Bern, Switzerland
UICC Conference on Clinical Oncology, October 28-31, 1981, Lausanne, Switzerland. International Union Against Cancer 131 pp., 1981.

Although the histogenesis of mediastinal germinomas is still unknown, circumstantial evidence indicates that these rare tumors may be derived from ectopic germ cells. We report on two cases characterized by the presence of germinoma tissue in the anterior mediastinum and high titers of serum antibodies against spermatopoietic cells. Patient 1, male, 21 yr, germinoma in an anterior mediastinal mass, operated and irradiated locally. He is well and alive 12 yr after operation. Patient 2, male, 24 yr, germinoma in an anterior mediastinal mass, tumor totally resected. No increase of alpha fetoprotein and beta human chorionic gonadotropin. At 8 mo post operative there was no evidence of disease. Serial dilutions of serum samples were tested by indirect immunofluorescence on non-fixed tissue for the presence of IgG-antibodies against germinoma cells as well as against allogeneic spermatopoietic cells of normal tests and testicular seminoma cells. In a total of 20 sera from patients with testicular seminoma antibodies against spermatopoietic cells were never detected. The presence of antibodies against germ cells in cases of mediastinal germinoma supports the interpretation that these tumors may be derived from spermatopoietic tissue. Since in our cases serum antibodies slowly disappeared after surgical removal of the tumors, serology may prove to be helpful tool in monitoring the follow-up of mediastinal germinoma. (no Refs)

CLINICAL/ DIAGNOSIS/ IMMUNOTHERAPY

17. CARCINOEMBRYONIC ANTIGEN (CEA) IN MAMMARY CARCINOMA: CLINICAL EVALUATION.

Villani C
Servizio di Oncologia, Universita di Roma, Rome, Italy
Minerva Med; 72(49):3315-3318,3320-3322 1981

Determination of carcinoembryonic antigen (CEA) for monitoring evolution and effect of therapy in mammary carcinoma (MC) was evaluated in 71 patients who were followed for 24 mo. Group A consisted of 48 early MC patients (T1-3N0-2M0; Stage I 8/48, Stage II 28/48, and Stage III 12/48). All the patients had surgery, followed by chemotherpy (CT) alone followed by the same CT combined with levamisole immunotherapy. Group B consisted of 23 advanced MC patients with metastases who were treated with palliative CT and CT associated with levamisole or CT associated with hormone therapy. Complete or partial remissions were achieved in 14/23; the remaining patients were unchanged or deteriorated. Determinations of CEA were performed 2-7 days before surgery, 15-30 days after surgery and every mo thereafter. CEA levels greater than 10 nanog/ml were found in 23/48 of early MC patients before surgery, in 13/48 after surgery, and in 16/23 with metastatic MC. Results in 48 patients in Group A were: 4 had consistently high CEA values (2 with relapse); 6 had increasing CEA values (4 with relapse); 12 had fluctuating CEA values (3 with relapse); 6 had normal CEA values, although CEA values were elevated immediately after surgery (1 with relapse but with CEA values in the normal range for greater than 1 yr); and 20 patients constantly maintained normal values. (23 Refs) (In ITA)

18. A CORRELATIVE STUDY OF CYTOLOGY AND CARCINOEMBRYONIC ANTIGEN DETERMINATION IN CEREBROSPINAL FLUID IN THE DIAGNOSIS OF BREAST CANCER CEREBRAL MENINGEAL METASTASES.

Fontaniere B, Ardiet C, Clavel M, Labaeche B, Clavel E, Faucon M
Laboratorie de Cytologie, Centre Leon-Berard, 28, rue Laennec, 69373 Lyon, France
Arch Anat Cytol Pathol; 29(5):287-290 1981

A study of cerebrospinal metastases in 53 women with breast cancer is reported. Of the 21 patients without any proven cerebral meningeal invasion, there were no positive results from cerebrospinal fluid (CSF) cytology or carcinoembryonic antigen (CEA). In 32 patients there was histological evidence of metastases. Of these, 21 showed positive results to cytodiagnosis and CEA testing. Of the 32 patients with metastases, 11 had normal cytology and no evidence of CEA in their cerebrospinal fluid. Of 14 patients who had several CSF examinations, 2/14 had normal levels of CEA in their serum and CSF even though cancer cells were observed in the CSF of one patient. In 8/14 the CEA levels in the CSF were abnormal and the CSF cytology was abnormal in 6/8. Positive CEA was found in the CSF of four patients whose serum was negative for CEA. Among these patients, 2/4 had positive CSF cytology. It is suggested that the disappearance of CEA from the CSF indicates clinical improvement during therapy. However, positive cytology can

sometimes reveal malignant proliferation during therapy. (15 Refs) (In FRE)

19. PROGNOSTIC SIGNIFICANCE OF CEA IN BREAST CANCER: A STATISTICAL STUDY.

de Jong-Bakker M, Hart AA, Persijn JP, Cleton FJ

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Eur J Cancer Clin Oncol; 17(12):1307-1313 1981

A statistical evaluation was carried out of serial CEA plasma levels in breast cancer patients. The study included 206 patients with operable primary tumor, 108 patients who were inoperable, 55 patients with advanced disease treated by oophorectomy and 77 post-menopausal patients treated with various endocrine regimens. The pretreatment CEA level was found to have no relation to prognosis. A rise in CEA during the follow-up period was usually associated with progressive disease. In 35% of the cases a rise in CEA preceded clinical signs of recurrence and metastases by an av of 200 days. The practical value of CEA in the management of breast cancer is limited because many tumors do not produce CEA. In CEA-producing tumors it provides a useful aid in clinical evaluation. The need for a strict statistical evaluation of CEA data in the follow-up of breast cancer patients is stressed. (Author abstract) (18 Refs)

20. CARCINOEMBRYONIC-LIKE SUBSTANCE IN BREAST FLUID DISCHARGE IN BENIGN AND MALIGNANT BREAST DISEASE AND IN MILK OF LACTATING WOMEN.

Kahana L, Bartal AH, Yechieli H, Guttman I, Sheinfeld M

Dept. Endocrinology, Kupat Holim, Lady Davis Carmel Hosp., 34362 Haifa, Israel

Isr J Med Sci; 17(11):1035-1040 1981

In a search for a simple noninvasive test for early detection of breast cancer, radioimmunoassay was used to determine carcinoembryonic (CEA) levels in the serum and breast fluid of 26 women presenting with spontaneous breast discharge, and in the serum and milk of 34 postpartum lactating women. In 54 milk samples from 34 healthy nursing mothers, the mean CEA level was 62.6 +-49.2 ng/ml (mean +- SD) (range 5 to 252 ng/ml). The highest levels were found during the first days after delivery. Serum CEA levels measured in 18 of the 34 mothers were negative in 12 cases and normal (10 +-5.3 ng/ml) in 6. No correlation was found between CEA levels in milk and those in serum. In the women with spontaneous breast fluid discharge, CEA levels in the breast fluid measured less than 300 ng/ml in 10 cases, 300 to 1,000 ng/ml in 9 cases and greater than 1,000 ng/ml in 7 cases. None of the 19 women with CEA values below 1,000 ng/ml had a malignancy. Four of the seven women with the highest CEA levels were found to have breast cancer. Serum CEA levels were within the normal range in both the malignant and nonmalignant cases. We conclude that CEA levels are markedly elevated in breast fluid discharges in nonlactating women, and that the highest levels may be associated with malignancy. (Author abstract) (22 Refs)

21. DELAYED EFFECTS OF ADJUVANT CYTOTOXIC CHEMOTHERAPY ON THE LYMPHOID SYSTEM AND BONE MARROW IN STAGE II BREAST CANCER (MEETING ABSTRACT).

Mackay IR, Riglar C, Kitchen PR, Collins JP, Goodyear MD
No affiliation given

Clinical Oncology Society of Australia, November 24-27, 1981, Melbourne, Australia. The Society 70 pp., 1981.

Thirty women with Stage II breast cancer given adjuvant cytotoxic chemotherapy for one yr with regimens including melphalan were studied to assess effects on bone marrow and immunological function, during and for up to three yr after cessation of therapy. There was long delayed recovery of blood cell numbers with leukocyte and platelet counts being significantly lower than pre-treatment values, even after three years. Correspondingly there was delayed recovery of counts in blood of T and B lymphocytes, but this was not reflected by functional tests relevant to the T cell system (delayed-type hypersensitivity (DTH) responsiveness and mitogenic responsiveness to phytohemagglutinin) or the B cell system (levels of immunoglobulins and isohemagglutinins, and flagellin antibody responses). There was no evidence of drug-induced interference with natural killer (NK) or K cell function. Prediction of recurrence was not afforded by any of the immunological indices except DTH responsiveness but was afforded by slowly-progressive increases in serum levels of carcinoembryonic antigen. The possibility of prolonged, albeit mild, depression of hemo- and lymphopoiesis should be a consideration in the selection of types and duration of adjuvant chemotherapy regimens, and in the extension of such regimens to types and stages of cancer with a lower likelihood of mortality. (no Refs)

22. SCINTIGRAPHY IN THE DIAGNOSIS OF THE SPREAD OF BREAST CANCERS (MEETING ABSTRACT).

Chatal JF
Centre R. Gauducheau, Nantes, France

Third Meeting of the French Society of Senology and Mammary Pathology, October 15-17, 1981, Versailles, France Centre Rene Huguenin; 1981

In 1981, ultrasonography and computed tomography are offering a serious challenge to the conventional radionuclide scan in the study of the metastatic spread of breast cancers to the liver and brain. There should nevertheless be a renewal of interest in the isotope method as a result of emission tomography which provides a two- or three-fold improvement in the contrast of pathological images as well as the possibility of three-dimensional images. There is also in prospect the clinical application of radiolabeled monoclonal antibodies directed against breast cancer cells. Initial studies using conventional anti-carcinoembryonic antigen (CEA) antibodies have been encouraging. (no Refs)

23. CARCINOEMBRYONIC ANTIGEN IN BREAST CARCINOMA (MEETING ABSTRACT).

Briere M, Brunet M, Gentile A, Gest J, Delaunay J, Gaches F, Hersant AM, Moulin G

Centre Rene Huguenin de Lutte Contre Le Cancer, Saint-Cloud, France

Third Meeting of the French Society of Senology and Mammary Pathology, October 15-17, 1981, Versailles, France Centre Rene Huguenin; 1981

After recapitulating some of the biochemical properties of carcinoembryonic antigen (CEA), we report studies on CEA in body fluids. With our radioimmunoassay, normal range was:

0 to 10 ng/ml. Results are reported on 314 breast carcinomas without perceptible metastases, without other cancerous localization, fully treated and supervised in our hospital. CEA in the serum, before treatment, is predictive of subsequent carcinologic events. This predictive aspect seems to be of value (grading III and negative axillary nodes (N-)). Comparison between the contents of CEA in effusion fluids and serum have been made and a correlation with cytology (Papanicolaou's classification) was established. It can be concluded that CEA assay is a complementary test with cytology for differentiating benign or malignant fluids. (no Refs)

24. SIMULTANEOUS FOLLOW-UP OF BREAST CANCER PATIENTS BY CARCINOEMBRYONIC ANTIGEN AND TISSUE POLYPEPTIDE ANTIGEN (MEETING ABSTRACT).

Luthgens M, Schlegel G, Schoen HD, Kruse-Jarres JD
No affiliation given
UICC Conference on Clinical Oncology, October 28-31, 1981, Lausanne, Switzerland. International Union Against Cancer 131 pp., 1981.

Breast cancer patients (227) were postoperatively followed by serum Carcinoembryonic Antigen (CEA) and Tissue Polypeptide Antigen (TPA) analysis. The patients were classified into four groups, 98 with no evidence of disease (NED), 39 with questionable evidence (QD), 17 with stable disease (SD), and 74 with progressive disease (PD). The clinical status of each patient was currently evaluated accompanied by simultaneous determination of CEA and TPA. In 89.2% of the PD courses TPA was found to be elevated and in 74.3% CEA. In 64.9% concordant elevations of both parameters were observed. In contrast, the NED group showed 12.2% elevations of TPA, 9.2% of CEA, in 4.1% concordant elevations. In the QD and SD groups 71% elevations of TPA were found, 36% of CEA, with 26% concordance of both parameters. Therapeutical responses of failures were better distinguished by the course of TPA than of CEA. There were seven cases, however, in which CEA behaved superior to TPA. Thus, a simultaneous follow-up of the post-operative course of breast cancer patients by CEA as well as TPA is advantageous to a monitoring by just one of the two parameters. By a simultaneous determination of CEA and TPA the total sensitivity amounts to greater than 95% and the specificity to 83%. (no Refs)

25. BIOCHEMICAL PREDICTION OF RECURRENCE IN PRIMARY BREAST CANCER (MEETING ABSTRACT).

Winkel P, Statland BE, Weis Bentzon M, Ammitzbol T, Mouridsen HT, Scheike O
Finseninstitute, 2100 Copenhagen, Denmark
UICC Conference on Clinical Oncology, October 28-31, 1981, Lausanne, Switzerland. International Union Against Cancer 131 pp., 1981.

In the prospective study of patients with primary breast cancer, blood and urine specimens were obtained at montly intervals following operation and stored at-80 C for later assay of 15 biochemical tumor markers. At present 16 of 69 consecutive patients have developed recurrence. The remaining 53 qualified as controls ie each one was without metastatic disease two yr following the time when the last blood specimen used in this study was obtained. A stepwise discriminant function analysis of initial postoperative clinical and biochemical data showed that only the number of positive nodes found at operation, the number of negative nodes, the grade of tumor anaplasia, urinary hydroxyproline and proline over creatinine contributed significantly to the discrimination between recurrence and controls. Autoregressive time series analysis of longitudinal data showed that only CEA detected recurrences without misclassifying controls. In using a conservative classification procedure, such that no controls were misclassified, 10 recurrences (62.5%) were detected. (no Refs)

26. THE INTER-RELATIONSHIPS BETWEEN CARCINOEMBRYONIC ANTIGEN (CEA) ESTROGEN AND PROGESTERONE RECEPTORS (ER), (PR) AND MORPHOLOGICAL CHARACTERISTICS IN HUMAN BREAST CANCER (MEETING ABSTRACT).

Sarfaty G, Nash A, Keightley D, Fisher R, Liddelow A
Prince of Wales Hospital, Randwick, New South Wales, Australia
Clinical Oncology Society of Australia, November 24-17, 1981, Melbourne, Australia. The Society 70 pp., 1981.

We have examined the ER, PR and CEA levels in the cytosol fraction of 119 histologically confirmed cases of primary breast cancer. ER was detected in 53%, PR in 28% and CEA in 63% of the tumors. Although presence of ER correlated significantly with PR, no significant correlation was found between CEA and ER. As ER and possibly PR correlate with morphological characteristics of breast cancer, their relationship and that of CEA was examined in 32 cases where complete histological data was obtained. Tumors were graded according to the World Health Organization Classification of Scarff and Torloni. ER was found to correlate with tumor grade, higher grades of tumor having fewer receptors. Although CEA and PR were also negatively associated with tumor grade neither relationship was statistically significant. No correlation was found between tumor fibrosis, necrosis, elastosis or lymphocytes and either CEA, ER or PR. While confirming from this study that breast cancer cytosol levels of ER are significantly associated with tumor grade, no such relationship exists for CEA and PR. Elevated plasma CEA is associated with advanced breast cancer in up to 73% of cases in some studies and is a marker for advanced disease. Whether cytosol CEA is a marker of prognosis independent of ER and tumor characteristics or is a function of tumor cell number is not revealed in the present data and requires further study. (no Refs)

27. INTEREST OF SOME BIOLOGICAL MARKERS IN THE PRELIMINARY STAGING OF BREAST CANCER (MEETING ABSTRACT).

Guiochet N, Reiss F, Gros D, Gairard B, Calderoli H, Keiling R
Service de Radiotherapie, Laboratoire de Cancerologie, Hospices Civils, 67091 Strasbourg, Cedex, France
Third Meeting of the French Society of Senology and Mammary Pathology, October 15-17, 1981, Versailles, France Centre Rene Huguenin; 1981

In 363 breast cancers diagnosed and treated between 10/1/79 and 7/1/81, we have determined before treatment 6 biological markers: carcinoembryonic antigen (CEA), beta human chorionic gonadotropin, alkaline phosphatases (PA), gamma glutamyl transferase (gamma GT), haptoglobine (H) and sedimentation speed (so called: VS). As the time is too short for survival study, we have compared the marker results to the tumor size (T) and histological positive nodes (N). The results pointed out that CEA is the only marker significantly correlated with T and N characteristics before treatment. In pathological CEA levels, there is no evident association with other prognostical factors as thermography, hormonal receptors and histoprognostical grading according to Scarff, Bloom and Richardson. Otherwise, the pathological CEA percentage is very low (10.4%), so the interest of this marker decreases as a prognostical factor and also in the follow-up of the disease. In fact, none of these markers is specific for breast cancer. (no Refs)

28. RADIOIMMUNOASSAY (RIA) IN PRIMARY BREAST CANCER: TISSUE AND PLASMA DETERMINATIONS (MEETING ABSTRACT).

Bartorelli A, Biancardi C, Ferrara R, Bailo M, Cavalca V, Accinni R
Istituto di Imunologia Clinica, Universita di Milano, Milan, Italy

UICC Conference on Clinical Oncology, October 28-31, 1981, Lausanne, Switzerland. International Union Against Cancer 131 pp., 1981.

We found a variable carcinoembryonic antigen (CEA)-like activity (RIA) in 80% of 48 primary breast carcinomas, singularly extracted (3 M KCl). Non-tumor tissues turned out negative. In the tissues with CEA-like activity indirect immunoperoxidase (PAP) showed cytoplasmic and membrane positivities stronger with antisera raised against BCA (Breast Cancer Antigen: CEA-like glycoproteins isolated form primary breast cancer tissue) than with those against CEA. The ratio between these two antisera is reversed when they are tested (PAP) against colon adenocarcinoma metastases. The difference in the immunological activity (RIA) between CEA and BCA is about 500-fold. Therefore a RIA technique, highly sensitive was developed to determine BCA extracted and partially purified, (bioabsorption chromatography, High Performance Liquid Chromatography) from 25 ml of plasma of each patient. (no Refs)

29. SIMULTANEOUS DOSAGE OF CEA, ALPHA FP AND BETA 2UG: ROLE IN THE MANAGEMENT OF BREAST CANCER (MEETING ABSTRACT).

Massant B, Fruhling J, Henry J
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UICC Conference on Clinical Oncology, October 28-31, 1981, Lausanne, Switzerland. International Union Against Cancer 131 pp., 1981.

The importance of several markers related with breast cancer is hardly discussed but few results have been published concerning the contribution of combined serological tests. Carcinoembryonic antigen (CEA), alphafetoprotein (alpha FP) and beta-2-microglobulin (beta2uG) are determined simultaneously in 94 breast cancer patients without generalization either after surgery and before radiotherapy (or radiochemotherapy), or before presurgical radiochemotherapy. Clinical staging gives stages I: 42 patients, II: 14, III: 36, unknown: 2. Anatomopathological staging gives 29 patients N-, 53 N+, 12 unknown. At the first determination, 48 patients (group A) have no abnormal value and 46 (group B) present at least one abnormal value (40 one abnormal value, 6 two). During the first yr, group A (with 29 patients with one yr follow-up) shows four generalizations (3N+, 1T4) and group B (with 20 patients with one yr follow-up) six generalizations and one death (6N+, 1 tumor left in place). An increase of beta2uG or CEA (from normal range to pathologic value) from 2 to 4 mo before clinical evidence of generalization is observed. In conclusion, these results suggest that combination of CEA and beta2uG might be useful for evaluation of breast cancer treatment, whereas interest of alpha FP does not appear. (no Refs)

30. THE ROLE OF FERRITIN AND CEA IN THE STAGING OF GASTRIC CARCINOMA (MEETING ABSTRACT).

Nitti D, Pagnini-Arslan C, Grassi F, Favretti F, Scarparo F, Lise M
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UICC Conference on Clinical Oncology, October 28-31, 1981, Lausanne, Switzerland. International Union Against Cancer 131 pp., 1981.

The clinical significance of Ferritin and Carcinoembryonic antigen (CEA) was stu died as a mean of staging in 65 gastric carcinoma patients. The preoperatory plasma levels of these markers were correlated to stage according to International Union Against Cancer and to some histological parameters (degree of differentiation, Lauren and Ming classification, vascular invasion, lymphocytic and peritumoral infiltration). The mean levels of Ferritin were all inside normal range. No correlation was found between Ferritin plasma levels and stage of disease. Besides serum Ferritin had no correlation with the histological parameters considered. In some cases pre and post operative Ferritine assays were useful to evaluate the efficacy of the treatment. Mean CEA levels were moderately higher in patients with 3rd and 4th stage but no statistical significant correlation was seen between CEA and stage or histological parameters. The utility of the repeated assays in the clinical follow-up was confirmed in some cases with preoperatory CEA levels increase. To conclude CEA and Ferritin are not important parameters in clinical staging of gastric carcioma. Only in a few cases CEA and Ferritin allow a valuation of the efficacy of the surgical treatment. (no Refs)

31. SIGNIFICANCE OF PREGNANCY-ASSOCIATED ALPHA 2-GLYCOPROTEIN IN PATIENTS WITH GASTRIC CANCER (MEETING ABSTRACT).

Shimizu Y, Ikuta K, Kato S, Oshima K, Nakano Y, Fujita M, Taguchi T
Department of Pathology, Osaka University, Osaka, Japan

Proceedings of the Japanese Cancer Association, 40th Annual Meeting, October 1981, Sapporo, Japan. The Association 415 pp., 1981.

We reported previously that pregnancy-associated alpha 2-glycoprotein (alpha 2 PAG) was a reliable marker for patients with breast cancer. In the present study, we analyzed the significance of alpha 2-PAG in patients with gastric cancer. In healthy controls, mean alpha 2-PAG values for females was statistically higher than that of males, so we discussed alpha 2-PAG values for males and females separately. Alpha 2-PAG levels were raised in patients with primary gastric cancer at any stage and remarkably increased in recurrent cases. This phenomenon can be detected indifferent to the histological types of gastric cancer. Raised alpha 2-PAG values were reduced gradually during 1-2 mo after curative surgery, but not in non-curative cases. These results showed that alpha 2-PAG might be a suitable marker for gastric cancer. Reliability of alpha 2-PAG as a marker was reinforced by the comparison of positive rates of three different parameters involving alpha 2-PAG, carcinoembryonic antigen and immunosuppressive acidic protein in patients and immunosuppressive acidic protein in patients with gastric cancer. To compare the alpha 2-PAG in sera of pregnant woman with that of patients with gastric cancer, we analyzed the sera by biochemical and immunological methods. A specific band with a mol wt of about 80,000 seemed to be alpha 2-PAG by immunoprecipitation and sodium dodecyl sulfate-polyacrylamide gel electrophoresis. (1 Ref)

32. CEA FOLLOW-UP IN GASTROINTESTINAL NEOPLASIA AFTER SURGERY.

Piantino P, Garrone C, Cattaneo U, Bonardi O, Toppino M, Pecchio F
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Minerva Dietol Gastroenterol; 27(4):541-545 1981

Carcinoembryonic antigen (CEA) was measured in 11 patients with gastric or colorectal carcinoma, before surgery, after surgery every mo during the first yr, every 3 mo for the following 3 yr, every 4 mo during yr 5 and 6, and once a yr thereafter. The patients had surgery for carcinoma (CA) of the rectum (5), large intestine CA (2), gastric CA (2), and degenerated gastric ulcer (2), all confirmed by pathologic examination. The greatest problem in the study was ensuring that patients came for follow-up examination. The study began with 50 patients, but only 11 cooperated. CEA determination cannot be used for diagnostic screening of CA, but it can show reaction to surgery, indicate early appearance of relapse or metastases, and indicate effects of chemotherapy. In all cases CEA values decreased after surgery; CEA continued to decrease in five cases. The CEA values increased in two cases, both beginning 4 mo after surgery. All patients who died showed elevated CEA values. (5 Refs) (In ITA)

33. VALUE OF PLASMA ALPHA-1-ACID GLYCOPROTEIN ASSAY IN THE DETECTION OF HUMAN COLORECTAL CANCER: COMPARISON WITH CARCINOEMBRYONIC ANTIGEN.

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JNCI; 68(1):75-79 1982

Plasma specimens assessed for carcinoembryonic antigen (CEA) in the clinical laboratory for the detection of colorectal cancer were simultaneously assayed in our laboratory for alpha-1-acid glycoprotein (alpha1AG), by means of a solid-phase enzyme-linked immunosorbent assay we developed. In 28 patients with colorectal cancer of Dukes A, B, and C classes, elevated levels of alpha1AG were seen in 12 and of CEA in 8. In 44 patients with distant metastasis (Dukes D lesions), elevated plasma levels of alpha1AG were seen in 29 and of CEA in 34. No statistical differences in the detection rate were found among these markers in these two groups of patients. In 33 cases of non-neoplastic disease involving the large bowel, elevated plasma levels of alpha1AG were seen in 6, and elevated CEA levels were seen in 7. There was no statistical difference of false positive rates among these two markers. Elevated plasma levels of either CEA or alpha1AG were found in 57 cases of colorectal cancer. This preliminary study suggests that the sensitivity of the plasma alpha1AG assay is similar to that of the CEA assay in the detection of colorectal cancer. The combination of these two assays increases the detection rate of colorectal cancer significantly. (Author abstract) (32 Refs)

34. PROGNOSTIC VALUE OF PREOPERATIVE SERUM CEA LEVEL COMPARED TO CLINICAL STAGING. I. COLORECTAL CARCINOMA.

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Br J Cancer; 44(5):652-662 1981

In a clinical investigation of observed postoperative survival, 563 patients have been registered for primary surgical treatment of colorectal cancer since 1974. The potential prognostic factors examined within the first days of hospitalization for primary resection included age of the patients, operability, location of the tumor, tumor extension and the preoperative serum CEA level. Statistical treatment of the data revealed that each of the clinical parameters except tumor location covers ranges associated with highly significant differences in survival of the patients. The preoperative serum CEA level gave prognostic information in addition to operability of tumor extension. The prognostic significance of the preoperative CEA level was still evident when selected subgroups of patients with distinct resectability and tumor extension were examined. The results indicate that the preoperative serum CEA level is an independent prognostic parameter. (Author abstract) (18 Refs)

35. THE VALUE AND LIMITATIONS OF CARCINOEMBRYONIC ANTIGEN LEVELS IN COLORECTAL CANCERS.

Grossetti D, De Certaines J, Trebuchet G, Auvray E, Bernard AM, Launois B
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Ann Chir; 35(10):875-877 1981

The value of monitoring carcinoembryonic antigen (CEA) levels in patients following colorectal carcinoma resection is discussed. Of 21 patients whose CEA level was greater than 100 nanog/ml, palliative surgery was performed in 16 cases and curative in 5 cases. Further surgical procedures included two abdominal perineal resections; (PAR) two hepatectomies, and one tumor reduction. One patient died 20 mo following PAR. The other patients were alive 3-18 mo following the second surgical procedure. In three cases in which exploratory laparotomy was performed widespread metastases prevented further tumor excision. The monitoring of CEA levels is recommended 2 mo postsurgery then every 6 mo for all Duke's Stage A, B, C patients who have undergone colorectal resection. A rising or stable CEA level indicates a search for local tumor recurrence or metastases despite the absence of clinical symptomatology. (24 Refs) (In FRE)

36. EXAMPLES FOR OUTPATIENT FOLLOW-UP CARE: COLORECTAL CARCINOMA: PROPOSAL BY ST. MARY'S HOSPITAL OF DUSSELDORF.

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MMW; 123(44):1657-1658 1981

A program for follow-up care of patients with colorectal carcinomas (CC) is presented. The program entails cooperation between the cancer clinic and the private physician and follows standardized investigative schemes and time schedules. Four programs are used: Program A consists of a history, clinical examination, and minor laboratory tests, including carcinoembryonic antigen (CEA) and occult blood tests. Program B consists of Program A plus major laboratory tests, endoscopy, and radiological studies. Program C consists of program B plus further radiological studies (including computer tomography, lymphography, and angiography) and nuclear medical studies of the bones and liver. Program D consists of Program C plus surgery. Six hundred twenty eight patients were treated under this programs. Of great significance was the determination of CEA titers. 'Second-look' operations were largely avoided. Tumor recurrence was found in 61/628 patients; a second curative operation was possible in only seven cases. Effective follow-up care of CC patients is important because of the rising incidence of CC, high responsiveness to therapy, and the possibility of curing recurrences. (no Refs) (In GER)

37. IN VIVO RADIOIMMUNODETECTION OF OCCULT RECURRENT COLONIC CARCINOMA.

DeLand FH, Kim EE, Primus FJ, Dine ME, Goldenberg DM
Veterans Admin., Lexington, KY, 40536
AJR; 138(1):145-148 1982

External imaging of radionuclide-labeled antibodies to carcinoembryonic antigen (CEA) was used to detect and localize metastatic carcinoma in a 57-yr-old woman with a rising and markedly elevated plasma CEA level 5 mo after anterior resection of an adenocarcinoma of the sigmoid colon. Other extensive radionuclide evaluations were not helpful in determining the cause of plasma CEA elevation. The value of in vivo radioimmunodetection for the demonstration of CEA-containing neoplasms is discussed. (16 Refs)

38. LOCALIZATION OF SUB-CLINICAL METASTASES OF COLORECTAL CARCINOMA BY RADIOIMMUNODETECTION (MEETING ABSTRACT).

Begent RH, Keep PA, Searle F, Dent J, Bagshawe KD, Jewkes RF, Jones BE, Vernon P
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UICC Conference on Clinical Oncology, October 28-31, 1981, Lausanne, Switzerland. International Union Against Cancer 131 pp., 1981.

Carcinomas of the colon and rectum can be localized by external scintigraphy after injection of 131 Iodine labelled antibody to carcinoembryonic antigen (CEA). It remains to be shown whether this method, Radioimmunodetection (RID) is sufficiently sensitive or specific to be clinically useful and this study describes investigation of 10 patients in whom recurrence after apparently curative resection was suspected because of abnormal serum CEA values. RID was performed by the method of Goldenberg et al in 10 such patients who had no clinical evidence of recurrence. RID was positive in 9, the sites being liver 3, liver and colon 1, liver and paraaortic nodes 1, liver and retrovesical area 1, perineum 1, bone 1, paracolic area 1. Intensive investigation of these sites subsequently led to unequivocal confirmation of the site of recurrence in 6 patients (4 by computerized tomography, 1 by ultrasound and 1 by surgery). These preliminary results suggest that RID may be of use in localization of early recurrence of colorectal cancer, being relevant to selection of patients for second-look surgery. (1 Ref)

39. STUDY OF ADJUVANT TREATMENT FOLLOWING SURGERY IN DUKES B2-C CARCINOMA OF LARGE BOWEL (MEETING ABSTRACT).

Rosso R, Sertoli MR, Parodi GC, Rubagotti A, Bonelli L
Istituto Scientifico per lo Studio e la Cura dei Tumori, Genoa, Italy
UICC Conference on Clinical Oncology, October 28-31, 1981, Lausanne, Switzerland. International Union Against Cancer 131 pp., 1981.

Survival of patients with B2-C colo-rectal carcinoma after surgery is significantly worse than for patients with A-B1 stages; this is why several studies have been carried out in order to verify the value of an adjuvant treatment. The results of two large controlled studies demonstrated the lack of efficacy of 5-FU employed in patients stage C as adjuvant treatment. On the other hand, several studies reported a significant advantage using the 5-Fluorouracil (5-FU) plus semustine (MeCCNU) combination in the advanced disease. On this background, in 1977 a randomized study has been started in our Institute in order to verify the value of the adjuvant treatment in B2-C stage patients using the 5-FU+MeCCNU combination. Moreover, the addition of an immunomodulating compound, Levamisole (L), has been evaluated for improving prognosis respect to chemotherapy alone (CT). A group of patients (group A) has been treated with Me-CCNU (150mg/mq po every 10 wk) + 5-FU (325mg/mq iv for 5 following days every 5 wk); a second group (group B) has been treated with the same chemotherapeutic combination plus L (150mg daily po for 3 following days during the second and the fourth wk of interval between successive chemotherapeutic cycles). Both groups have been treated for 14 cycles. Patients have been monitored by clinical, radiologic and scans evaluations, besides usual blood examinations and carcinoembryonic antigen. A preliminary evaluation at 18 mo showed a difference for either survival or disease free survival in the CT+L arm; the difference was not significant because of the low number of evaluable patients (15 for each group). A recent update of the study will be pre sented showing no benefit in terms of survival and disease free survival for the chemo-immunotherapy versus the CT alone. (no Refs)

40. EPIDEMIOLOGICAL AND IMMUNOLOGICAL ASPECTS OF GASTROINTESTINAL CANCER IN ISRAEL (MEETING ABSTRACT).

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Unit of Oncology, Department of Medicine, Kaplan Hospital, Rehovot, Israel

UICC Conference on Clinical Oncology, October 28-31, 1981, Lausanne, Switzerland. International Union Against Cancer 131 pp., 1981.

Gastrointestinal (GI) cancer in Israel is significantly less common among Jews of Oriental (O) origin compared to Jews of European (E) origin. The purpose of our study was to determine whether such differences were in any way related to the immune functions. In a propective study of 188 newly diagnosed GI cancer patients several immune parameters were determined and correlated with disease stage and course and with the ethnic background. Patients were studied preoperatively and every 4 mo subsequently. Age, sex and ethnic backgroud matched controls were studied in parallel. The main positive findings were: a) Increased spontaneous (background) thymidine uptake of peripheral blood lymphocytes of (0) vs (E) patients accounting also for differences observed in the response to mitogens between the two ethnic groups; b) Higher grade of malignancy as assessed by nuclear grading in (0) vs (E) patients; c) A trend for more immune reactivity at tumor site among (0) vs (E) patients. In addition, a) The diagnostic efficacy of the leucocyte adherence inhibition assay (LAI) in the preoperative diagnosis of colorectal carcinoma was 31/54 (57%) and this rate increased to 70% when it was combined with determination of carcinoembryonic antigen. b) Antinuclear antibodies (ANA) were more common among patients and correlated with tumor dissemination. c) No significant differences were found between the various groups in the circulating immune complexes and blood lymphoid populations. It would thus seem that stronger immune reactivity towards the tumor is present in the Oriental host and would possibly explain why this ethnic group is better protected from GI cancer. (no Refs)

41. TENNESSEE ANTIGEN AND THE MONITORING OF PATIENTS WITH COLORECTAL CANCER (MEETING ABSTRACT).

Walker CT, Gray BN
Department of Surgery, St. Vincent's Hospital, Fitzroy, Victoria, Australia
Clinical Oncology Society of Australia, November 24-17, 1981, Melbourne, Australia. The Society 70 pp., 1981.

Tennessee Antigen (TennaGen) was used to serially monitor patients bearing neoplasms of the colon and rectum who had had potentially curative resections. These results were then compared with Carcinoembryonic Antigen (CEA) determinations in the same patients. Thirty-six patients were selected to be studied. Nineteen patients had a Dukes' B tumor. Seventeen patients had Dukes' C tumors. Twenty-six of these patients have recurred, while ten show no evidence of recurrence. TennaGen was measured by hemagglutination inhibition, the principle of which is the inhibition of agglutination of an antigen-antibody reaction by a second antigen. Thirty-one patients had preoperative assays of both TennaGen and CEA. Twenty-nine had an elevated TennaGen, but only nine had an elevated CEA. Post-operatively all patients that recurred had elevated TennaGen. All ten disease free patients also showed elevated levels. In both groups of patients there was little change between pre and post-operative levels. CEA became elevated in 22 of 26 patients that recurred and gave lead in times of up to 12 mo. Tennessee Antigen was found to be of no value in the monitoring of potentially cured patients with malignancies of the large bowel due to its high false positive rate and its lack of sensitivity and specificity while CEA was found to be of value. (no Refs)

42. A NEW CONCEPT ON THE NATURAL COURSE OF HEPATOCELLULAR CARCINOMA.

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Chin Med J [Engl]; 94(9):585-588 1981

The natural course of hepatocellular carcinoma (HCC) was followed-up in a group of patients who received nonresectional treatment. Seventeen patients had subclinical HCC, 87 had moderate stage HCC, and 50 had late stage HCC. During greater than 1-yr follow-up, the patients were subjected to serial determinations of alpha-fetoprotein (AFP) levels. Median survival of the patients with late stage HCC was 2 mo, compared with 6 mo for moderate stage and 14 mo for subclinical stage. The median duration of survival from the first appearance of low AFP level (greater than 50 nanog/ml) was 24 mo. Analysis of HCC patients subjected to resection showed the median sizes of the tumor in subclinical. moderate, and late stages of HCC of 3.5, 9.0, and 10.0 cm, respectively. The increase in tumor size was correlated with AFP level. These findings indicate that HCC has a relatively long natural course and that the concept of 'acute malignancy' represents the late stage of HCC. (8 Refs)

43. SEROLOGIC PROFILE AND POSSIBLE ETIOLOGIC FACTORS IN PRIMITIVE CARCINOMA OF THE LIVER.

Caporaso N, Giardullo N, Servillo F, Del Vecchio-Blanco C, Coltorti M
Istituto di Semeiotica Medica, I Facolta di Medicina e Chirurgia, Universita di Napoli, Napoli, Italy
Fegato; 27(1):55-57 1981

The relationship between primitive carcinoma of the liver (PCL) and chronic infection with virus B (CIVB) was studied using radioimmunoassay. CIVB seems to play an important role in the etiology of PCL, especially in areas of high incidence of CIVB. Of 612 patients with evolutive liver pathology, 32 (36-83 yr old, 27 men and 5 women) had PCL. In 23 patients PCL was associated with cirrhosis (ALC); of these 9 had acute progressive hepatitis, 6 were alcoholics, and 7 had blood relatives who had died from PCL. Diagnosis was confirmed by biopsy (obtained through laparoscopy). scintigraphy, alpha1-fetoprotein, and routine blood chemistry. Nine patients had negative results for all serological markers, 11 had positive results for HBsAg+, 4 for anti-HBc+, and 8 for both anti-HBc+ and anti-HBs+. Of the 11 HBsAg+ positive cases, only 2 were associated with 'e' positive results, indicating that the infection with virus B had occurred long ago. No patients reported exposure to toxic industrial products, or contaminated food, or prolongued use of sexual hormones or their derivatives. PCL was frequently associated with CIVB even in non-ALC cases. (5 Refs) (In ITA)

44. ASPIRATION CYTOLOGY IN THE DIAGNOSIS OF LIVER CANCER.

De Cock KM, Gatei DG, Shah MV
Dept. Medicine, Kenyatta Natl. Hosp., Nairobi, Kenya
East Afr Med J; 58(9):636-640 1981

Diagnostic efficacy of liver aspiration was evaluated in 31 patients (28 men, 3 women; 25-65 yr old) with suspected liver cancer. Among these patients, 29 had either histological proof of hepatocellular carcinoma, positive alpha-fetoprotein assay, or positive ultrasound liver scan. Cytological examination of fine needle liver aspirates showed malignant cells in 27/29 patients. An overall false positive rate was 6.5%. (10 Refs)

45. CLINICAL CLASSIFICATION OF HEPATOMA IN JAPAN ACCORDING TO SERIAL CHANGES IN SERUM ALPHA-FETOPROTEIN LEVELS.

Matsumoto Y, Suzuki T, Asada I, Ozawa K, Tobe T, Honjo I
Dept. Surgery, Kohka Medical Center, Minakuchi, Shiga, 528, Japan
Cancer; 49(2):354-360 1982

Quantitative determinations of serum alpha-fetoprotein (AFP) in 96 patients with hepatomas have demonstrated three main groups based on changes in the serial levels: (1) patients with more than 10,000 ng/ml or more in a wk (Group A); (2) patients with levels varying from 200 to 10,000 ng/ml and with an increase of 1,000 ng/ml in 3 to 4 mo (Group B); and (3) patients with serum aFP levels below 200 ng/ml during most of their clinical course (Group C). The patients in Group A had a mean survival time of 7.62 +-2.97 mo, and those in Group B, 16.18 +-12.18 mo. The patients in Group C were subdivided into two groups according to whether survival time was long (33.92 +-28.22 mo) or short (3.75 +-0.87 mo). Histologic findings revealed poorly differentiated carcinoma in patients in Group A, moderately differentiated carcinoma in those in Group B, and well differentiated carcinoma in those with long survival in Group C and anaplastic carcinoma in those with short survival in Group C. (Author abstract) (15 Refs)

46. TREATMENT OF HEPATOCELLULAR CARCINOMA BY INTRA-ARTERIAL INFUSION WITH MITOMYCIN C.

Nishioka M, Noda K, Fukumoto Y, Kodama T, Okita K, Shigeta K, Nishimura H, Harada T, Takemoto T
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Bull Yamaguchi Med Sch; 28(1/2):57-62 1981

Twenty-nine patients with hepatocellular carcinoma (PHC) were given oral administration of 5-Fluorouracil (or Futraful) and intermittent intra-arterial infusion with 10-20 mg of Mitomycin C (MMC). Objective responses such as decreased serum alpha-fetoprotein level, decrease in the liver size, and prolongation of the survival time were found in 15, 14, and 13 out of 29 patients respectively. Subjective symptoms such as weakness, abdominal pain, and loss of appetite were improved in 7 of 29 patients. Of control patients with PHC who received oral administration of 5-Fu (or Futraful) alone, or intravenous injection of 4 mg of MMC twice a wk, the objective responses were observed in 1 of 13 patients. This indicates significant therapeutic effect of intra-arterial infusion of MMC on patients with PHC. Patients with severe liver dysfunction, decreased number of peripheral lymphocytes, or high level of serum alkaline phosphatase were unsuitable for this infusion. A significant decrease of serum hemoglobin level was observed as a side effect of intra-arterial infusion of MMC. (Author abstract) (12 Refs)

47. OBSERVATIONS ON CHANGES OF SERUM A-FETOPROTEIN (AFP) LEVELS IN 632 NORMAL INFANTS.

Shen W, Xu Y, Sheng J, Xu F
Inst. Pediatrics, Shanghai First Medical Coll., Shanghai, People's Republic of China
Zhonghua Erke Zazhi; 19(2):96-97 1981

Elevated serum alpha-fetoprotein (AFP) levels observed in liver cancer and other diseases have been used in the diagnosis of liver cancer for over 10 yr. Using the radio-rocket electrophoresis autoradiographic method, serum AFP levels were analyzed for 632 normal infants (319 males, 313 females; 23 days-2 yr 8 mo old). They were found to be highly elevated in newborn infants (median value greater than 1,000 nanog/ml) but gradually fell to normal adult levels (less than 31 nanog/ml) 3 mo after birth. It was concluded that serum AFP cannot be used in diagnosing disease in infants aged less than 3 mo, because the normal elevated levels in these infants would be misleading. (6 Refs) (In CHI)

48. USE OF MULTIPLE TUMOUR MARKERS IN THE SCREENING FOR EARLY PRIMARY HEPATOCELLULAR CARCINOMA IN THE POPULATION IN SINGAPORE (MEETING ABSTRACT).

Oon CJ, Chio LF, Singh R, Chan L, Lim GK, Yo SL
Department of Medicine, National University of Singapore, Singapore General Hospital, Singapore 0316, Singapore
UICC Conference on Clinical Oncology, October 28-31, 1981, Lausanne, Switzerland. International Union Against Cancer 131 pp., 1981.

From 1979-1981 an ongoing prospective study was done on high-risk groups of the population in Singapore to determine the incidence of the primary hepatocellular carcinoma (PHC) in the various at risk groups. The groups studied were: 1000 normal males over 40 yr, 160 immediate PHC family members, 80 cirrhosis, 60 chronic hepatitis B carriers, 250 women on oral contraceptives and 50 males on androgen replacement therapy. Tumor markers used were Alphafetoprotein (AFP) (CIE), alpha1 antitrypsin (ATT), alpha1acidglycoprotein I, gammaglutamyl transpeptidase (GGT), and isocitrate dehydrogenase. Three of 1000 normal male population, (0.3%), 4/160 family PHC members (2.5%), 30/80 (38%) cirrhosis, 6/60 (10%) chronic hepatitis B carriers and 4/150 (1.6%) women on estrogen progesterone pills developed PHC. Hepatomegaly, (not due to a medical cause) was caused by PHC in 45/80 (56%) of patients. No male patients on normal androgen replacement therapy developed PHC after 3 yr follow up. AFP, ATT and GGT remain the most useful detector for PHC. Specific isoenzymes of ATT and GGT may be more useful in differentiating PHC from other conditions. Raised ATT levels in pill takers returned to normal on discontinuation. Only 10% of detectible tumors were resectible. All tumors detectible preclinically were 10 cm diameter (+/-) 2 cm. Three of 3 (100%) of these patients are alive at 1 yr follow up. (no Refs)

49. CORRELATION OF 3 TUMOUR MARKERS (CALCITONIN, CEA AND BETA-HCG) WITH RESPONSE TO THERAPY AND EXTENT OF DISEASE IN SMALL CELL LUNG CANCER (MEETING ABSTRACT).

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UICC Conference on Clinical Oncology, October 28-31, 1981, Lausanne, Switzerland. International Union Against Cancer 131 pp., 1981.

Plasma levels of 3 tumor markers (calcitonin, carcinoembryonic antigen (CEA) and beta human chorionic gonadotropin (HCG)) were measured at presentation in 40 patients with small cell lung carcinoma to investigate whether there was any correlation with response to chemotherapy and extent of disease. Ten patients (25%) had raised calcitonin, 15 (38%) raised CEA and 7 (18%) raised beta-HCG levels. Twenty patients (50%) had no abnormal markers. The response rate achieved with chemotherapy was related to the number of raised markers: of the 22 patients who responded, 19 had 0-1 marker raised, whereas only 2 had 2-3 markers raised. Strikingly only 2 out of the 10 patients with elevated calcitonin responded to therapy. The extent of disease at presentation correlated with the number of raised markers: 15 out of the 30 patients with 0-1 marker raised had extensive disease, compared with 8 out of the 10 with 2-3 markers raised. In particular 12 out of the 15 patients with elevated CEA had extensive disease. There were, in addition, 28 patients whose plasma was taken during the course of their disease and not at presentation: 27 out of 68 (40%) had raised calcitonin and 41 out of 68 (60%) had normal values. The proportion of extensive disease and the overall response rate were similar in both groups, but interestingly, only 3 patients out of the 27 (11%) with raised calcitonin achieved a complete response to chemotherapy whereas 14 out of the 41 (34%) of the calcitonin negative group did so. These results indicate that certain tumor markers may help to predict response to therapy in patients with small cell lung cancer, with important prognostic implications. (no Refs)

50. CORRELATIVE TENDENCY BETWEEN CEA VALUES AND NUCLEAR DNA MODAL VALUES IN HUMAN LUNG TUMORS (MEETING ABSTRACT).

Ozaki HS, Yoneyama T, Hoshino K
Department of Anatomy, Kyoto University, Kyoto, Japan
Proceedings of the Japanese Cancer Association, 40th Annual Meeting, October 1981, Sapporo, Japan. The Association 415 pp., 1981.

CEA, Carcinoembryonic antigen has been studied as a tumor marker and a possible parameter of clinical features in neoplasia. Our purpose was to find any correlations between CEA values in blood sera and nuclear DNA contents measured cytofluorometrically in lung tumors. By analyzing DNA modal values in each tumor, the nuclear DNA distribution patterns appear to be classified into three major types: Diploid-Tetraploid type, Triploid type and Mixed type. A correlative tendency was found: Serum CEA values are higher in the patients with lung tumors of Triploid or Mixed type than in the patients with Diploid-Tetraploid type tumors. This suggests that CEA values seem to be correlated with the degrees of malignancy of human lung tumors. (no Refs)

51. BIOLOGICAL MARKERS FOR TUMORS OF THE TESTIS: THEIR USE IN DIAGNOSIS PROGNOSIS AND FOLLOW-UP IN 200 CASES.

Bellet D, Caillaud JM, Droz JP, Delarue JC, Bohuon C
Service de Biologie Clinique, Inst. Gustave Roussy, F 94800 Villejuif, France
Nouv Presse Med; 10(40):3293-3297 1981

Repeated measurements of serum chorionic gonadotrophic hormone (CGH) of its beta sub-unit (beta-CGH) and of alpha-fetoprotein (aFP) were performed in 200 patients with germinal tumors of the testis. CGH levels were found to be high in 43.5% of patients, particularly those with choriocarcinoma (a rare tumor) or with embryonal carcinoma with syncytiotrophoblastic (ST) cells. They were also high in 24% of patients with histologically pure seminoma, which throws doubts on the homogeneity of this group of tumors and raises problems concerning their treatment in patients with high CGH. aFP levels were increased in 38% of all patients, particularly those with ST cell embryonal carcinoma (62%) or with malignant teratoma (56%). These biochemical markers may point to a histological diagnosis. They also have prognostic value and are essential for monitoring during treatment. Pre-operative assays are of particular interest and should be performed in every case. (Author abstract) (22 Refs) (In FRE)

52. TUMOR MARKERS HCG AND AFP IN TESTICULAR SEMINOMAS (MEETING ABSTRACT).

Bombardieri E, Pizzocaro G, Pilotti S, Lattuada A, Cozzi A, Bruni GF, Buraggi GL
INT, Milan, Italy
UICC Conference on Clinical Oncology, October 28-31, 1981, Lausanne, Switzerland. International Union Against Cancer 131 pp., 1981.

Usually pure seminoma is considered to be rare alpha fetoprotien (AFP) and a poor human chorionic gonadotropin (HCG) producer. Ninety-nine patients with pure testicular seminoma have been studied for serum HCG. Forty-eight patients were disease free when first examined and all had negative serum HCG. Seventeen in the 51 disease bearing patients (33.3%) had elevated HCG serum levels. Histology was reviewed and new sections examined in these 17 cases: in 11 of them (64.7%) sincityal giant cells were singled out optically. Morphological features different from the ones typical of seminoma were found in 15 out of 17 patients. In our series there was no correlation between stage of the disease and serum HCG levels, and no significant difference in prognosis has been observed among patients with and without elevated HCG in the same stage group. Only four patients with seminoma had elevated AFP: 2 had liver disease. Histology was reviewed in the remaining 2 cases: one showed an area of embryonal carcinoma among seminomatous tissue, and the other had atypical seminoma, with positive staining for AFP immunoperoxidase. Our experience suggests that 1/3 of apparently pure seminomas is HCG secreting. HCG positive seminomas are usually atypical, and in an occasional case these tumors may also produce AFP. (no Refs)

53. PROGNOSTIC FACTORS IN TESTICULAR CANCER: ALPHA-1-FETOPROTEIN (AFP), HUMAN CHORIONIC GONADOTROPIN (HCG) HLA ANTIGENS (MEETING ABSTRACT).

Aiginger P, Schwarz HP, Zahler J, Kirsch K, Kuzmits R, Keuhboeck R, Mayr WR, Spona J
2nd Department of Medicine, Institute of Blood Serology and Institute of Pathology, Vienna, Austria
UICC Conference on Clinical Oncology, October 28-31, 1981, Lausanne, Switzerland. International Union Against Cancer 131 pp., 1981.

Fifty-six patients (pts) with testicular germ-cell tumors received either vinblastine-bleomycin or vinbl-bleom-cisplatinum. Two yr follow up proved to be comparable in both groups (45 and 47% complete remissions, CR). Therefore pts of both groups were considered together when alpha fetoprotein (AFP) and human chorionic gonadotropin (HCG) serum concentrations and HLA antigens were evaluated for their importance as prognostic factors. Pts with AFP values above 500 ng/ml (15% CR,) had significantly reduced chances of achieving a CR, whereas elevated HCG levels had no similiar impact on the CR rate. In 62 pts were evaluated for 14 HLA-A, 21 HLA-B and 5 HLA-C locus antigens. Twenty-five pts were also examined for HLA-DR antigens. The antigens frequencies of HLA-B13 (20 vs 5%) and HLA-A10 (A25 +26: 31 vs 13%) were significantly elevated in the teratoma group as compared with the normal controls and the seminoma group. The incidence of HLA-B13 was highest in the HCG pos subgroup of the melignant teratomas. Further analyses reveiled that all pts with HLA-A24 and 10/11 pts with HLA-B13 had metastatic disease. No differences were detected so far in the incidences of the HLA-DR antigens. (no Refs)

54. EARLY DETECTION OF RELAPSE BY ALPHA1-FETOPROTEIN, BETA-HCG AND LDH IN NONSEMINOMATOUS TESTICULAR TUMORS (MEETING ABSTRACT).

Scheulen ME, Pfeiffer R, Schmidt CG
West German Tumor Center, Essen, W. Germany
UICC Conference on Clinical Oncology, October 28-31, 1981, Lausanne, Switzerland. International Union Against Cancer 131 pp., 1981.

The course of disease had been monitored by clinical control and determination of alpha-fetoprotein (AFP), beta human chorionic gonadotropin (HCG) and lactic dehydrogenase (LDH) in 230 patients with nonseminomatous testicular tumors. Clinical controls included physical examination, serial chest roentgenogram and abdominal ultrasonography. AFP and/or beta-HCG were initially elevated in 176/230 patients (77%). Elevation of AFP, beta-HCG and/or LDH was the first sign of recurrence of disease in 27/44 patients in complete remission (61%) preceding its clinical detection between 1 and 8 mo (mean 2.6 mo). Relapses were first detected by AFP and/or beta-HCG in 20/44 patients (45%) and by LDH in 7/44 patients (16%). LDH was particularly useful in the early diagnosis of relapses in 4/13 initially tumormarker-negative patients (31%). Altogether, only in 6/44 patients (14%) recurrence of disease was detected by clinical control prior to AFP-, beta-HCG- and/or LDH-elevation. In conclusion, routine determination of AFP, beta-HCG and LDH is an essential tool in the early detection of relapse in patients with nonseminomatous testicular tumors. (no Refs)

55. ESTROGENS AS A NEW MARKER OF TESTICULAR CARCINOMA (MEETING ABSTRACT).

Schmoll HJ, Muhlen AV
Division of Hematology, Medical School Hanaover, Hannover, W. Germany
UICC Conference on Clinical Oncology, October 28-31, 1981, Lausanne, Switzerland. International Union Against Cancer 131 pp., 1981.

In 172 patients (pts) with nonseminomatous testis cancer (39 stage I, 42 stage IIa/b, 91 stage IIc - IIIb) serial determinations of beta human chorionic gonadotropin (HCG), alpha fetoprotein (AFP), lactate dehydrogenase (LDH), luteinizing hormone (LH), follicle stimulating hormone (FSH), prolactine, E1, E2, total estrogen, T3, T4, rT3 have been done. An elevation during the course of the disease was observed in 62% with AFP, in 54% with betaHCG, 34% with LDH, 64% with E1, 67% with E2, 39% with total estrogen. Elevation during no evidence of disease (NED) time of FSH, E1, or E2 was followed by clinical progress in 40% of the pts; elevation of total estrogen to the 2-fold of normal predicted a clinical process of the disease with recurrence in 70%, an elevation to the 3-fold in 96%, with a median time of 3 mo until the clinical sign of the disease. Sixty-seven percent of these pts are dead with tumor, indicating the worse prognosis against pts without estrogen elevation. T3, T4, rT3 always are in the normal range, with 15 pts showing increasing T3 or T4. The data suggest that a) estrogens are produced by testicular carcinoma, b) the estrogen determination is useful for the following up of testis cancer pts, and c) estrogen production with significant elevation of the serum level is a sign of poor prognosis. (no Refs)

56. OFA-1 DISTRIBUTION IN GYNECOLOGICAL CANCER TISSUES: ANTI-OFA-1 IN CANCER PATIENTS (MEETING ABSTRACT).

Higuchi M, Takahashi M, Takeuchi Y, Hando T, Takeuchi S
Department of Obstetrics and Gynecology, Niigata University School of Medicine, Niigata, Japan
Proceedings of the Japanese Cancer Association, 40th Annual Meeting, October 1981, Sapporo, Japan. The Association 415 pp., 1981.

The immunogenic oncofetal antigen (OFA-1) was discovered during studies on the characterization of membrane antigens of human melanomas. To study the distribution of OFA-1 in cancer and trophoblastic tissues is potentially valuable in its clinical application. Ovarian cancer, 100% (4/4), had the highest prevalence of OFA-1. Cervical cancer was OFA-1 positive in 40% (2/5). In comparison, uterine cancer, trophoblast and hydatidiform mole were OFA-1 negative. Further, anti-OFA-1 was detected in sera of 90.0% (20/22) of choriocarcinoma, 37.4% (21/56) of cervical cancer, 50% (10/20) of ovarian cancer, 100% (5/5) of dysgerminoma and 60% (3/5) of vulvar cancer. (no Refs)

57. THE PROGNOSTIC VALUE OF CEA MEASUREMENTS IN PATIENTS WITH CARCINOMA OF THE UTERINE CERVIX TREATED WITH RADIATION THERAPY (MEETING ABSTRACT).

Braun P, Leyendecker G
University-Frauenklinik, Bonn, W. Germany
UICC Conference on Clinical Oncology, October 28-31, 1981, Lausanne, Switzerland. International Union Against Cancer 131 pp., 1981.

Serum levels of carcinoembryonic antigen (CEA) were determined radioimmunologically (Cis-Kit) in 50 patients suffering from carcinoma of the uterine cervix stage III during and after radiation therapy for up to three yr. Initial CEA levels were elevated (above 12 ng/ml) in 52% of the patients. CEA levels before treatment had no prognostic value as far as median survival time was concerned. In contrast, CEA levels measured immediately after therapy in patients with initially elevated levels turned out to be of prognostic significance. When the posttreatment concentrations of CEA were found to be in the normal range, the median survival time was 835 days. When the CEA levels remained to be elevated, however, the median survival time was only 256 days. Seventy-four percent (14/19) of the patients, who developed recurrent cervical cancer or persistent disease, had progressively increasing CEA levels. A progressive rise of serum CEA preceded the clinical diagnosis of recurrence by 1 to 6 mo. We conclude that in patients with elevated pretreatment levels CEA concentrations after therapy provide an important prognostic criterion and that CEA measurements may be used as an additional tool in the follow up of patients suffering from carcinoma of the uterine cervix. (no Refs)

58. THE PROGNOSTIC VALUE OF CEA DETERMINATION IN OVARIAN CANCER (MEETING ABSTRACT).

Malkin A, Malkin DG, Sturgeon JF, Kellen JA
Sunnybrook Medical Centre and Princess Margaret Hospital, Toronto, Canada
UICC Conference on Clinical Oncology, October 28-31, 1981, Lausanne, Switzerland. International Union Against Cancer 131 pp., 1981.

The prognostic value of initial and sequential carcinoembryonic antigen (CEA) tests following surgery was evaluated in 326 patients with ovarian cancer participating in an ongoing clinical trial. The initial CEA was determined within one to three mo following surgery and at least four tests extending over six mo were performed serially on all patients. Survival data showed that patients with a normal initial CEA had a better prognosis than those with an abnormal CEA. This was not surprising since the initial CEA test reflects tumor burden. Stratifying by stage, we noted that the prognostic significance of an initially elevated CEA held true whether the patients belonged to Stages 1 and 2 or Stages 3 and 4. Also, looking at the serial data, patients with a persistently elevated CEA do worse than those with a persistently normal CEA whether in Stages 1 and 2 or Stages 3 and 4. Finally patients with a persistently normal CEA do better than those with a CEA which is normal initially but which rises to abnormal levels subsequently, whether in Stages 1 and 2 or Stages 3 and 4. We conclude that: (1) the CEA is a prognostic indicator of survival, independent of stage, in patients with ovarian cancer as with cancer of the bowel, breast and lung and (2) in the organization of clinical trials, this fact should be taken into account in the stratification process before randomization into treatment arms especially if the prognostic value of the test in ovarian cancer is found to be independent of other prognostic factors such as histopathology and amount of residual disease following surgery. (no Refs)

59. CORRELATION OF SINGLE AND SERIAL CEA DETERMINATIONS WITH THE CLINICAL EVOLUTION OF CANCER PATIENTS.

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Centro Medico de Prevencion y Tratamiento, Viamente 2565, Buenos Aires, Argentina
Arch Geschwulstforsch; 52(2):105-112 1982

Correlations between single or serial determinations of carcinoembryonic antigen (CEA) and clinical progress of breast or colorectal cancer were studied. Patients included 41 with breast cancer (BC) and 15 with colorectal cancer (CRC) and were in various stages of disease after surgery and radio- or chemotherapy. Among BC patients initial CEA determination corresponded to clinically observed stage of disease in 75% of cases. Two cases were termed 'real false results'. One with increased CEA and no symptoms later developed a recurrence. Serial CEA determinations were made over a 4-yr period. Two or more consecutive findings in the same direction corresponded to clinical findings in 93% of cases. Among CRC patients initial CEA determinations agreed with clinical findings in 12 cases. Two cases were real false results. Patients with normal CEA showed favorable prognosis; no change in therapy was indicated by single CEA findings above normal but less than 3x max normal values; two or more abnormal findings indicated progression of disease. CEA determination for a period of at least 1 yr is recommended in combination with other clinical tests and physical examinations for follow-up of patients with BC or CRC. (12 Refs)

60. RESULTS OF CEA DETERMINATION IN CASES OF SQUAMOUS CELL CARCINOMA OF THE MAXILLOFACIAL AREA.

Hardt N, Steinhausen EW, Bloch B
Abteilung fur Kiefer-Gesichts-Chirurgie, Chirurgische Klinik, Kantonsspital Luzern, CH-6004 Luzern, Switzerland
Dtsch Zahnaerztl Z; 36(11):767-770 1981

The value of determinations of carcinoembryonic antigen (CEA) levels for diagnosis and therapy control in cases of squamous cell carcinomas (SCC) of the maxillofacial area was studied. A retrospective review of 480 patients indicated that, with a false negative rate of 48%, CEA levels provided no useful information for diagnosis. In individual cases changes in CEA levels correlated well with response to treatment in 50-70% of cases. An original study of 20 patients [12 treated by surgery and 8 treated by primary or secondary chemotherapy (CT) or radiotherapy (RT)] confirmed the prognostic value of CEA determinations. Postoperative observation period was 2-24 mo. Among surgically treated patients five showed a decrease in CEA levels to normal values, three showed a decrease within the pathological range, and four showed no correlation between CEA levels and therapy response. Tumors recurred in three patients, of whom two showed increased CEA levels. Increases in CEA appeared 3-4 wk before recurrence was apparent. Among eight patients receiving CT and/or RT, six showed a correlation between CEA levels and therapy response (four with decreased levels and tumor regression and two with increased levels and tumor progression), and two showed no correlation. Results indicate that CEA determinations, in combination with other indicators, are useful for supervision of therapy of maxillofacial SCC. (20 Refs) (In GER)

61. EVALUATION OF CARCINOEMBRYONIC ANTIGEN (CEA) IN PATIENTS WITH HEMATIC CANCER.

Bulfoni A
II Divisione Medica, Ospedale Civile di Udine, Udine, Italy
Arch Sci Med (Torino); 138(4):449-454 1981

Carcinoembryonic antigen (CEA) was evaluated in 47 patients with non Hodgkin's lymphoma 12, Hodgkin's lymphoma (HL) 9, chronic lymphatic leukemia (CLL) 6, chronic myeloid leukemia (CML) 3, plasmacytoma (PC) 6, idiopathic myelofibrosis 2, polycythemia vera 2, and 21 patients with cancers of endodermal tissues (gastric 8, bronchogenic 7, pancreatic 4, and colorectal 2). The CEA determinations were performed using radioimmunoassay. Of 47 patients with hematic cancer, 10 had CEA values above 20 nanog/ml. These 10 patients had HL (4), CLL (2), PC (2), non HL (1), and CML (1). The highest value of CEA (320 nanog/ml) was observed in one case of CLL, which was complicated with primary hepatic carcinoma. The CEA values were negative in 37 (79%) of 47 patients and independent of the phase of the disease. Of the 21 patients with cancers of entodermal tissues, 76% had CEA values above 20 nanog/ml, and quantitatively the CEA values were higher than in the 10 hematic cancer patients. (35 Refs) (In ITA)

62. SERUM CARCINOEMBRYONIC ANTIGEN LEVELS IN PATIENTS WITH APUDOMA.

Fujiyama S, Oishi S, Umeda T, Sato T
Third Dept. Internal Medicine, Kumamoto Univ. Medical Sch., Kumamoto City, Japan
Jpn J Clin Oncol; 11(3):427-430 1981

Concentration of serum carcinoembryonic antigen (CEA) was measured by radioimmunoassay in 26 patients with various types of apudomas (pheochromocytoma (11), Sipple's syndrome (2), medullary carcinoma of the thyroid (MCT: 2), parathyroid adenoma (2), neuroblastoma (5), insulinoma (1), glucagonoma (1)). Values in 142 controls suggested 2.5 nang (ng)/ml as the upper normal limit. All four patients with Sipple's syndrome and the two with MCT showed moderate or marked elevation of CEA of 3.6-34.5 ng/ml. Two of 11 patients with pheochromocytoma had marginally elevated values. One of five with neuroblastoma and one with insulinoma had slightly elevated values. Levels in the patient with glucagonoma and two with parathyroid adenoma were within normal limits. It is concluded that CEA level cannot be used as a tumor marker in all apudomas but it is valuable and specific for MCT. (6 Refs)

63. DETERMINATION OF CARCINOEMBRYONIC ANTIGENS IN THE BLOOD IN BULLOUS AND GENETICALLY DETERMINED DERMATOSES.

Krause W, Stahl N
Zentrum fur Dermatologie und Andrologie, Klinikum der Justus-Liebig-Universitat, Gaffkystr. 14, D-6300 Giessen, W. Germany
Hautarzt; 32(12):632-633 1981

Blood levels of carcinoembryonic antigen (CEA) were measured in 82 patients with bullous, vesicular, or hereditary dermatoses and in 30 healthy controls. Mean CEA values for various disease forms studied were all within the range of values for controls, 10.3-42.1 nanog/ml, although some individual values were outside this range. Data do not support the contention that some dermatoses are accompanied by increased CEA levels. (8 Refs) (In GER)

ULTRASTRUCTURE/ CYTOCHEMISTRY

64. CARCINOPLACENTAL ALKALINE PHOSPHATASE IN MALIGNANT AND PREMALIGNANT CONDITIONS OF THE HUMAN DIGESTIVE TRACT.

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Virchows Arch [Pathol Anat]; 394(1/2):109-118 1981

The presence of carcinoplacental alkaline phosphatase (CP Alk P) was demonstrated in the cells of malignant and premalignant states of the human stomach, colon and rectum using the immunoperoxidase technique. It was shown to be present in 7 out of 18 carcinomas of stomach and 7 of 17 cases of carcinoma of colon and rectum. In the putative premalignant states it was demonstrated in 4 of 15 cases of intestinal metaplasia associated with gastric carcinoma, and 9 of 12 tubulovillous adenomas of colon. However, it was also demonstrated in five of eight metaplastic polyps of colon which are neoplastic and in 9 of 17 cases of intestinal metaplasia not associated with cancer of the stomach. It was not seen in normal gastric mucosa and only faintly in 1 of 11 samples of normal colon. CP Alk P has been shown to be a specific marker of malignancy in a wide range of human cancers when studied in sera from patients or in tissue culture of tumor cells. In this study however, although a statistical difference exists between normal and diseased tissue the marker appears as frequently in non-neoplastic states. It is concluded that CP Alk P is, in tissues, a marker of proliferative activity in cells, rather than neoplastic or malignant change. In this respect it is similar in some respects to carcinoembryonic antigen, but not other markers of placental origin such as pregnancy specific beta, glycoprotein. (Author abstract) (20 Refs)

65. CLINICAL AND PATHOLOGICAL CHARACTERISTICS OF GRANULAR CELL TUMORS IN THE AREA OF THE MOUTH, JAW, AND FACE.

Ploke G, Caselitz J, Maerker R
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Dtsch Zahnaerztl Z; 36(11):732-734 1981

Clinical and pathological findings in seven cases (4 males and 3 females, newborn up to 75 yr old) of granular cell tumors (GCT) of the orofacial area are reported. None of the patients had received prior treatment. Tumors were 0.5-3.0 cm in size. Two tumors were located on the skin; two were on the tongue; three were on the maxilla. Two maxillary tumors were congenital epulis. Tumors were tolerated or unnoticed for long periods because they were generally small and not painful. Diagnosis required differentiation from disorders such as fibroma, neurofibroma, papilloma, mucosal cysts, hyperplasias of secondary salivary glands, and malignant lymphoma. Laboratory findings were unexceptional. Therapy consisted of simple excision after intraoperative histologic examination. All tumors had indistinct borders lacking a capsule. Histologic examination showed round, oval, or elongated cell forms. Cell cytoplasm was eosinophilic or neutrophilic and contained PAS-positive granules. Carcinoembryonic antigen was detected by immunohistologic methods, suggesting that GCT does not originate from muscle cells, but may be related to perineural cells. No recurrence was noted during an observation period of 1-6 yr. (13 Refs) (In GER)

66. IMMUNOHISTOCHEMICAL DETECTION OF CARCINOEMBRYONIC ANTIGEN (CEA) IN PAROTID GLAND CARCINOMAS: ANALYSIS OF 52 CASES.

Caselitz J, Jaup T, Seifert G
Inst. Pathology, Univ. Hamburg and Tumour Center Hamburg, Martinistrasse 52, D-2000 Hamburg 20, W. Germany
Virchows Arch [Pathol Anat]; 394(1/2):49-60 1981

The presence of CEA in parotid gland tumors was studied by immunohistochemical methods. Fifty-two cases were analyzed. Seven of eight adenocarcinomas, three of five cystadenocarcinomas, three of four adenoid cystic carcinomas and all three salivary duct carcinomas were positive for CEA. Five of eight squamous cell carcinomas and 9 of 21 carcinomas in a pleomorphic adenoma were also positive for CEA. The anaplastic carcinomas were negative. The distribution pattern of the presence of CEA in the carcinomatous and the adjacent normal or inflamed tissue was analyzed. The results are discussed with regard to their histogenetic and diagnostic implications. (Author abstract) (37 Refs)

67. CARCINOEMBRYONIC ANTIGEN IN CARCINOMA OF THE UTERINE CERVIX: ANTIGEN DISTRIBUTION IN PRIMARY AND METASTATIC TUMORS.

van Nagell JR, Hudson S, Gay EC, Donaldson ES, Hanson M, Powell DF, Goldenberg DM
Gynecologic Oncology, Univ. Kentucky Medical Center, 800 Rose St., Lexington, KY, 40506
Cancer; 49(2):379-383 1982

Immunohistochemical staining for carcinoembryonic antigen (CEA) was performed on primary tumors and regional lymph nodes from 100 patients undergoing radical hysterectomies and pelvic lymphadenectomies for invasive carcinoma of the uterine cervix. Antigen staining was present in 82% of keratinizing squamous carcinomas as compared with 50% in nonkeratinizing tumors. Seventeen patients with CEA-producing cervical cancer had regional lymph node metastases, all of which stained positively for CEA. Conversely, antigen could not be detected in lymph nodal metastases from primary tumors devoid of CEA. The pattern and intensity of CEA staining in primary tumors and their metastases were similar in all cases. Antig en was present in highest concentrations in the cytoplasm and tumor cell membrane of all tissues examined and isolated nuclear staining was absent. The clinical implications of these findings are discussed. (Author abstract) (21 Refs)

68. AN UNLABELED ANTIBODY METHOD USING GLUCOSE OXIDASE-ANTIGLUCOSE OXIDASE COMPLEXES (GAG): A SENSITIVE ALTERNATIVE TO IMMUNOPEROXIDASE FOR THE DETECTION OF TISSUE ANTIGENS.

Clark CA, Downs EC, Primus FJ
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J Histochem Cytochem; 30(1):27-34 1982

Immunoenzyme staining for tissue antigens using glucose oxidase as marker enzyme was compared with immunoperoxidase techniques. Both the indirect, conjugated antibody method and the unlabeled antibody procedure employing preformed complexes of glucose oxidase-antiglucose oxidase (GAG) and peroxidase-antiperoxidase (PAP) were used to stain carcinoembryonic antigen (CEA) in paraffin tissue sections. The localization of CEA within a tissue specimen was the same in all cases, and background staining was minimal. The percentage of positive specimens detected with GAG and PAP was similar but was slightly greater with glucose oxidase compared to peroxidase conjugates. The glucose oxidase conjugates and GAG were similar to the comparable immunoperoxidase reagents in enzyme-antibody molar ratio, retention of antibody and enzyme activity, immunohistochemical staining dilutions, and stability. Immunoglucose oxidase and immunoperoxidase were combined to localize CEA and colon-specific antigen-p simultaneously. Excellent contrast and staining separation were shown between the enzymatic reaction products of the two systems. Since immunoglucose oxidase methods are as sensitive as the comparable immunoperoxidase techniques, they should be considered as a reliable alternative to the latter, especially when endogenous peroxidase activity may be a problem. Furthermore, the two methods can be conveniently combined for the simultaneous detection of two antigens. (Author abstract) (35 Refs)

69. EPITHELIAL MEMBRANE ANTIGEN (EMA): ITS VALUE IN DIAGNOSTIC CYTOLOGY (MEETING ABSTRACT).

Dearnaley DP, To A, Ormerod MG, Coleman DV
Ludwig Institute for Cancer Research, Sutton, Surrey SM2 5PX, England
UICC Conference on Clinical Oncology, October 28-31, 1981, Lausanne, Switzerland. International Union Against Cancer 131 pp., 1981.

The distinction between reactive mesothelial and malignant cells in cytological specimens is a frequent cause of diagnostic difficulty. In order to determine whether an immunocytochemical method might resolve these difficult cases, we have stained smears of 309 serous effusions from 246 patients for the Epithelial Membrane Antigen (EMA). The EMA staining was classified as strong, weak or negative. Carcinoma cells (as diagnosed by conventional cytology) stained strongly for EMA in 63 of the 112 positive smears. In contrast only 2 out of 121 cytologically negative smears from patients without malignant disease contained cells with a strong EMA stain. This shows that expression of high concentrations of EMA is strongly suggestive of malignancy. Of particular interest were three effusions in which malignant cells were not identified by a conventional screen and in which a small number of EMA positive cells were identified. After a subsequent Papanicolou stain, malignant cells were identified on retrospective morphological examination. Further studies using antiserum to carcinoembryonic antigen and pre-keratin may define roles for these markers in diagnostic cytology. (no Refs)

REVIEWS/ OTHER RELATED STUDIES

70. TUMOR DIAGNOSIS WITH IMMUNOLOGICAL METHODS.

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ZFA (Stuttgart); 57(3):177-186 1981

Tumor diagnosis by immunological methods is reviewed. Determination of tumor-associated antigens has the following general applications: (1) in cases of suspected primary hepatic carcinoma or malignant testicular tumors, alpha-feto-protein should be measured, (2) for suspected carcinoma of the gastrointestinal tract, pancreas, or biliary tract, or for detection of recurrence or metastasis, carcinoembryonic antigen (CEA) should be determined, (3) for suspected carcinoma of the head of the pancreas, CEA and beta-2-microglobulin should be measured simultaneously in the duodenal fluid, rather than in the serum, and (4) for suspected bronchial, mammary, or female genital carcinoma, hypernephroma, or sarcoma, tissue polypeptide antigen, with or without CEA, should be determined. Individual cases may require additional tests, such as hormone or enzyme determinations, for diagnosis. None of the immunologic tests is definitive in all cases. Most are economically feasible in normal usage. Application of immunological diagnostic methods to clinical practice are discussed. (23 Refs) (In GER)

71. SCREENING FOR COLORECTAL CANCER.

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J Fam Pract; 12(4):625-632 1981

The efficacy of various screening techniques for diagnosis of colorectal cancer is evaluated from studies in the literature. Consideration is given to principles of screening. Some techniques have been abandoned, such as carcinoembryonic antigen, while others, such as colonic mucin staining, are still being developed. Sigmoidoscopy and tests for occult blood are discussed. While sigmoidoscopy (with the rigid instrument) may occasionally aid in detection of early curable cancer, it has limitations and is unacceptable in subjects without symptoms of bowel disease. The test for occult blood is now institutionalized as the guaiac-impregnated Hemoccult Slide, which is safe and acceptable to those involved. The Hemoccult test presents problems with respect to sensitivity in those with negative results, and is influenced by the number of slides used, control of diet (red meat, vitamin C), and rehydration of dried smears. Data from Hemoccult testing are inconclusive. Until newer techniques, such as flexible sigmoidoscopy, immunologic markers, and colonic mucin stains become established, available tests should be used efficiently. (57 Refs)

72. SPECIFIC CELL SURFACE CHANGES IN BREAST CANCER: DETECTION IN THE BLOOD OF THE TUMOR HOST (MEETING ABSTRACT).

Braecker HP
Department of Obst and Gyn, RWTH Aachen, D-5100 Aachen, W. Germany
UICC Conference on Clinical Oncology, October 28-31, 1981, Lausanne, Switzerland. International Union Against Cancer 131 pp., 1981.

The malignant transformation of a mammalian cell is known to be a very complex process. There is good evidence that among other effects it causes a change of the cell's surface protein coat. Preparation of cell surface proteins from 12 mammary carcinomas of various histological appearence were performed by hypertonic salt extraction with 3 M KCl. These extracts were further analyzed by analytical isoelectric focusing along with matched blood samples from the tumor hosts. Specimen of blood and tissues from patients with benign breast disease served as controls. It could be demonstrated that each tumor had its specific pattern of surface proteins which differed significantly from non-malignant breast tissue. At least in part, these aberrant proteins could be detected in corresponding samples of the tumor host's serum, but never in sera from healthy controls. It was shown that these new proteins do not belong to the oncofetal antigens carcinoembryonic antigen (CEA) or alpha fetoprotein (AFP). The results suggest that there are certain specific changes on the surface of breast cancer cells which are detectable in the tumor host's blood and may provide a more sensitive tool in the patient's follow up. (no Refs)

73. USE OF TUMOR MARKERS (CEA) (MEETING ABSTRACT).

Wanebo HJ
No affiliation given
Current Concepts in Cancer Therapy, December 10-12, 1981, St Louis, Missouri Washington University School of Medicine; 1981

Although the carcinoembryonic antigen (CEA) is not specific for colorectal cancer, its strong correlation with many aspects of the disease has made it very useful in the clinical management of this malignancy. There is controversy, however, about the real value of CEA determinations in the clinical decision-making process, and the impact on patients prognosis. This review analyzes the relative values of the preoperative CEA, postoperative monitoring of CEA levels, the correlation of CEA with different patterns of recurrence, and the potential for detecting early recurrence and selecting patients for second-look surgery. There is suggesive evidence that the preoperative CEA may be of value as a prognostic indicator complementing clinical pathologic staging. Patients with elevated preoperative CEA are at higher risk for recurrence than those with lower preoperative values. In patients who developed liver metastasis the CEA elevation commonly preceded the clinical or other laboratory evidence for disease, whereas patients who developed local recurrence commonly had clinical evidence of disease prior to a rise in CEA. Sequential CEA tests are a useful monitor for recurrence and to identify patients who might be good candidates for second-look surgery. In general, the CEA usually returned to normal by the second wk after resection. In collected published series from four institutions recurrence was documented in 78% to 94% of 86 patients who had undergone second-look surgery because of a rising CEA. There was marked variation among institutions regarding patient population, frequency of CEA testing and willingness to perform second-look surgery primarily on the basis of CEA. Long-term survival results are not yet available. Because of the variation in the collected series it is worth reviewing the experience of the Ohio Stage Group which pioneered the approach and has been most aggressive in applying CEA directed second-look surgey. In a recent update which includes their retrospective and prospective data, 60 patients have undergone operation, of whom 56 (93%) had tumor confirmed. Of the 35 patients in the 'prospective' study, 60% had resectable tumor and 21 (35%) are currently free of disease. (no Refs)

74. FROM DIAGNOSIS TO PROGNOSTIC AND TREATMENT OF BREAST CANCER (MEETING ABSTRACT).

Gest J, Turpin F
Centre R. Huguenin, Saint-Cloud, France
Third Meeting of the French Society of Senology and Mammary Pathology, October 15-17, 1981, Versailles, France Centre Rene Huguenin; 1981

The frequency of breast cancer justifies the research for technics of best diagnostic value, allowing an early diagnosis and the determination of prognostic factors, without being too heavy for the patient and expensive for the society. For each technic, its qualities of reproducibility, sensitivity and predictive value must be measured. Pathology plays a preeminent role in the definition and diagnosis of breast cancer and 'precursor mastopathies'. The histological type, the Scarff Bloom and Richardson grading, and the diffusion of carcinomatous process are the more valuable prognostic factors which will modify the treatment. Practically, the diagnosis of breast cancer needs the research of risk factors, personal and familial, a clinical examination leading to the tumor, node, metastasis (TNM) classification, always completed by a mammography and cytological study of the tumor and lymph nodes and finally a per operative histological examination. The research for metastasis will rely on lung x-ray examination, bone scannogram, gamma glutamyl transferase (GT) and carcinoembryonic antigen (CEA) levels, and if abnormal, liver echotomography. Our works must aim toward a strict definition and classification of carcinomas and 'precursor mastopathies', the use only of technics with best diagnostic performances, the knowledge of cost and iatrogenicity of these technics, and must lead to the prevention of the disease. (no Refs)

75. UTERINE SARCOMAS (MEETING ABSTRACT).

Grey JW, Cope I, Osborn RA
No affiliation given
Clinical Oncology Society of Australia, November 24-27, 1981, Melbourne, Australia. The Society 70 pp., 1981.

This study is a review of 41 patients with diagnosed uterine sarcoma. The histories and pathology from two Sydney teaching hospitals were reviewed at the Royal Hospital for Women, Paddington. They covered the period from 1962 to 1981. Eight cases previously diagnosed as leiomyosarcomas were found to be bizarre or cellular leiomyomata. Despite the marked cellular pleomorphism and nuclear atypia within the group, prognosis was directly related to the mitotic figure rate. On histological classification there were 14 cases of leiomyosarcoma, 14 malignant mixed Mullerian tumors, two Mullerian adenosarcomas and one low grade endometrial sarcoma (endolymphatic stromal myosis). The av survival time for the group was 18 mo. There was a marked variation in the primary method of treatment chosen for all stages of the disease. Two of the surviving patients had surgery and chemotherapy as primary treatment for stage one disease. Adriamycin remains the cornerstone of chemotherapy treatment. Recent results of combination regimens (Vincristine and Adriamycin plus cyclophosphamide or dacarbazine, DTIC) appear very encouraging. The overall poor prognosis and early distant metastases indicates that chemotherapy is an essential part of treatment, particularly for early stage disease. Estrogen and progesterone receptor identification should be performed on all these tumors. In some reported cases carcinoembryonic antigen (CEA) levels have proved valuable in assessing response and recurrence. (no Refs)

76. ENZYMATIC LABELING OF CARCINOEMBRYONIC ANTIGEN WITH IODINE-125.

Siuda A, Lucka B, Russin K
Radioisotope Production and Distribution Center, Inst. Nuclear Res., Swierk 05-400 Otwock, Poland
J Labelled Comp Radiopharm; 18(12):1797-1807 1981

Lactoperoxidase was used to label carcinoembryonic antigen (CEA) from human hepatic metastases of colonic carcinoma with 125-I. Labeled CEA was purified by gel permeation chromatography and isolated by Sephacryl-S-200 column chromatography. Approx three I atoms were incorporated per CEA molecule; 125-I CEA retained 0.6 of its original immunological activity after 2 mo, and was stable at room temperature. (17 Refs)

77. EFFECT OF ANTI-AFP ANTIBODY-DAUNOMYCIN CONJUGATE ON THE GROWTH OF AFP-PRODUCING TUMOR CELLS (MEETING ABSTRACT).

Hibi N, Tsukada Y, Hara A, Hirai H
Department of Biochemistry, Hokkaido University School of Medicine, Sapporo, Japan
Proceedings of the Japanese Cancer Association, 40th Annual Meeting, October 1981, Sapporo, Japan. The Association 415 pp., 1981.

Specific antibody to rat alpha-fetoprotein (AFP) was linked to daunomycin via dextran bridge. The drug and antibody activity of the conjugate retained over 50 percent of that of free drug or antibody. Specific cytotoxicity of the conjugate was revealed by the inhibition of tumor growth in vitro as well as in vivo. The conjugate also possessed the effect of diminishing the drug toxicity. (no Refs)

78. THE RESPONSE OF LYMPH NODE METASTASES OF NONSEMINOMATOUS GERM CELL TESTIS CANCER TO CHEMOTHERAPY AND INDICATIONS FOR SUBSEQUENT SURGERY (MEETING ABSTRACT).

Vugrin D, Whitmore WF, Golbey RB
Memorial Sloan-Kettering Cancer Center, New York, NY
UICC Conference on Clinical Oncology, October 28-31, 1981, Lausanne, Switzerland. International Union Against Cancer 131 pp., 1981.

The role of urologic surgeon in the treatment of retroperitoneal metastases after chemotherapy for stage III nonseminomatous germ cell testis cancer is evaluated. Fifty-one patients with stage III disease, who were treated with one of the vinblastine, actinomycin D, bleomycin (VAB) chemotherapy protocols, had retroperitoneal metastases (RPM) at the beginning of chemotherapy. RPM were considered advanced (ARPM) if patients had deviation of ureter on iv pyelogram, a palpable mass, or mass with diameter greater than 5 cm, documented at surgery or by computed tomography. Patients with lesser metastatic deposits were considered to have minimal RPM (MRPM), 13 patients had MRPM and all achieved complete remission (CR) with chemotherapy alone (Ch CR), 38 patients had ARPM and only 10 (26%) had Ch CR. Patients with teratomatous elements (T) in the testis tumor had lower Ch CR than those without T. Patients with bulky RPM had teratoma in primary tumor more frequently than those with MRPM. Thirty-four percent (13/38) patients with ARPM and incomplete response to chemotherapy entered CR after complete resection of residual disease (SCR). T was present in testis and RPM in 10, and in RPM but not in testis in 3. Most of the patients who could not be salvaged (15) with chemotherapy and/or surgery had ARPM, T in primary tumor (8) or elevated alpha fetoprotein (4) in serum possibly suggesting T in RPM. We conclude that the presence of teratomatous elements in testis tumor in patients with stage III disease and RPM is associated with lower CR with chemotherapy alone, and such patients are candidates for adjuvant surgery. Patients with bulky RPM usually have T in the testis tumor, have a low Ch CR, and should have RPLND after 3 induction courses of chemotherapy. Patients with MRPM will usually achieve Ch CR and may not need RPLND. (no Refs)

79. CEREBROSPINAL FLUID: A SELECTIVE REVIEW.

Cutler RW, Spertell RB
Dept. Neurology, Stanford Univ. Sch. Medicine, Stanford, CA, 94305
Ann Neurol; 11(1):1-10 1982

Selected areas in which analysis of cerebrospinal fluid may elucidate brain disease are reviewed. Biochemical markers of CNS malignancy are discussed. The lysosomal and microsomal enzyme beta-glucuronidase has been reported to be elevated in the lumbar fluid of patients with meningeal carcinomatosis. Carcinoembryonic antigen, the beta-subunit of human chorionic gonadotropin, alpha-fetoprotein, and glial fibrillary acidic protein may also mark CNS malignancy. (175 Refs)

80. CYTOGENETIC ANOMALIES IN A PATIENT WITH ATAXIA, IMMUNE DEFICIENCY, AND HIGH ALPHA-FETOPROTEIN IN THE ABSENCE OF TELANGIECTASIA.

Ying KL, Decoteau WE
Childrens Hosp. Los Angeles, 4650 Sunset Blvd., P.O. Box 54700, Los Angeles, CA, 90054
Cancer Genet Cytogenet; 4(4):311-317 1981

A 58-yr-old male with spinocerebellar degeneration in association with choreiform movement is described. He possessed neurological, biochemical, immunological, as well as cytogenetic disorders predisposing to cancer similar to patients with ataxia telangiectasia (AT). Cytogenetic abnormalities included four abnormal clones: trisomy 14;t(13;14);t(7,14)(q32;q12); and t(7;14)(p13;q12), in addition to breaks, rings, and acentric chromosomes. The absence of telangiectasia, the late onset of neurological symptoms, and the prolonged survival in this case may separate it from the classic AT. Although the syndrome may be recognized as a new chromosome instability syndrome, multiple allelism may play a role in the expression of a milder form of AT. (Author abstract) (19 Refs)

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EXPERIMENTS IN ANIMAL SYSTEMS

1. ISOLATION OF ALPHA-FETOPROTEIN MESSENGER RIBONUCLEIC ACID FROM AH-66 ASCITES HEPATOMA CELLS.

Choi NH, Higashi T
Dept. Biochemistry, Sch. Pharmaceutical Sciences, Showa Univ., 1-5-8, Hatanodai, Shinagawa-ku, Tokyo, 142, Japan
Chem Pharm Bull (Tokyo); 29(11):3305-3310 1981

The messenger (m)RNA for alpha-fetoprotein (AFP) was isolated from polysomes of AH-66 rat hepatoma cells by extraction of immunoprecipitates and purification by affinity chromatography with oligo(deoxythymidine)-cellulose column. Sodium dodecyl sulfate polyacrylamide gel electrophoresis of AFP gave two mol wt peaks of 72,000 and 74,000; the purified AFP contained 1.5% hexose, 1.5% hexosamine, and 0.9% sialic acid. Electrophoresis of purified AFP mRNA on acid-urea agarose gel suggested a mol wt of 2,700. Purified anti-AFP antibody from anti-rat AFP horse antiserum was reactive against AH-66 ascites fluid, purified rat AFP, and anti-horse IgG rabbit antibody, but not adult rat serum. A quantitative analysis showed that the molar ratio of anti-AFP antibody to

HE 20.3173/

rat AFP is approx one at the equivalent point. Purified AFP mRNA translated in the wheat germ S-30 cell-free system was measured by radioactivity incorporated in immunoprecipitates; results indicated that the obtained AFP mRNA was at least 75% pure in terms of messenger activity. (21 Refs)

2. STUDIES ON THE ACTIVITY OF ALPHA-FETOPROTEIN GENE.

Choi NH, Higashi T

Dept. Biochemistry, Sch. Pharmaceutical Sciences, Showa Univ., 1-5-8 Hatanodai, Shinagawa-ku, Tokyo 142, Japan

Chem Pharm Bull (Tokyo); 29(11):3311-3319 1981

Purified alpha-fetoprotein (AFP) messenger (m)RNA from rat AH-66 hepatoma cells formed complementary (c)DNA upon incubation in a system with avian myeloblastosis virus RNA-dependent DNA polymerase. The (3H)cDNA had a peak fraction of about 1,000 nucleotide length upon alkali-sucrose gradient centrifugation; AFP cDNA hybridized with AFP mRNA, but not with rat liver catalase mRNA. Thermal denaturation analysis showed a sharp melting profile, indicating a faithful transcription in AFP cDNA:mRNA hybrids. The conformation of the AFP gene was studied by digestion of nuclei of AH-66 cells and rat liver cells with DNAse I or microsomal nuclease. Chromosomal proteins (CP) extracted from chromatin of AH-66 and rat liver cells were similar in comparisons by QAE-Sephadex A-25 chromatography and sodium dodecyl sulfate-polyacrylamide gel electrophoresis. RNA transcripts from intact and reconstituted chromatin of AH-66 cells hybridized with AFP cDNA, but those from rat liver cells did not, indicating that AFP gene is active in AH-66 cells, but suppressed in liver cells. The addition of one of the fractions of AH-66 CP during reconstitution of rat liver chromatin lead to transcription of the AFP gene; no rat liver CP could be found that when added during reconstitution would inhibit transcription of AH-66 AFP gene. (24 Refs)

3. REGULATION OF RAT ALPHA-FETOPROTEIN PRODUCTION BY METHIONINE DURING ETHIONINE-HEPATOCARCINOGENESIS.

Miyazaki M, Watanabe A

Div. Pathology, Cancer Inst., Okayama Univ., Okayama 700, Japan

Int J Cancer; 29(2):213-216 1982

The levels of serum alpha-fetoprotein (AFP) in rats were determined during hepatocarcinogenesis with ethionine, and the effects of methionine administration on serum AFP elevation in these animals were studied with the aim of investigating regulatory mechanisms of AFP production during carcinogenesis. Elevation of serum AFP was observed 6 wk following the start of feeding a diet containing 0.25% ethionine and again at the 22nd wk of feeding, when a well-differentiated hepatoma had already developed. These biphasic elevations of serum AFP concentrations in rats fed a 0.25% ethionine-containing diet decreased abruptly and significantly following a change to the basal diet either supplemented with or without 0.7% methionine. The possibility that regulation of AFP production in these rats may correlate with methionine metabolisms is discussed on the basis of the experimental data obtained. (Author abstract) (17 Refs)

4. MONOCLONAL ANTIBODIES TO TWO MOUSE BLADDER CARCINOMA ANTIGENS.

Hellstrom I, Rollins N, Settle S, Chapman P, Chapman WH, Hellstrom KE

Program Tumor Immunology, Fred Hutchinson Cancer Res. Center, Seattle, WA, 98104

Int J Cancer; 29(2):175-180 1982

Carcinomas of the urinary bladder of mice were induced by 3-methyl-cholanthrene or FANFT [(4-5-nitro-2-furyl)-2-thioazolyl formamide]. On transplantation in vivo, tumor lines consisting of well-differentiated transitional-cell carcinomas were established. Some tumors were also explanted in vitro. A rat was immunized with a pool of carcinomas and normal bladder tissue and its spleen cells were hybridized with NS-1 mouse myeloma cells. Supernatants of hybrid cells ('hybridomas') were screened for antibody binding to antigens present in bladder carcinomas but not in normal syngeneic urinary bladder, with cell extracts as targets. Hybridomas that appeared to have the required specificity were cloned, tested further against transitional-cell bladder carcinomas, an anaplastic bladder tumor, rhabdomyosarcomas, a mammary carcinoma, myelomas and lymphomas, and normal adult urinary bladder, kidney, lung, spleen, heart, brain, thymus, and whole embryo. Antibody formed by one hybridoma, 2H5, gave significant binding to membranes from five of seven transitional-cell carcinomas but not to membranes from any other tissues. A second hybridoma, IE6, formed antibody to an antigen present in bladder carcinomas and normal liver and, in smaller amounts, in several other normal and neoplastic tissues. Fluorescence microscopy established that both antigens were present at the cell surface of transitional-cell bladder carcinomas. Immunoprecipitation and SDS-polyacrylamide gel electrophoresis were used to identify the target antigens from 125I-labeled cell membrane proteins. The antibody formed by 2H5 was found to identify a protein with a mol wt in the range of 140 kilodaltons, which was detected in transitional-cell bladder carcinoma and, in small amounts, in normal bladder. The molecular nature of the antigen defined by hybridoma IE6 is not known. (Author abstract) (25 Refs)

5. ALKALINE PHOSPHODIESTERASE I AND ALKALINE PHOSPHATASE I IN PLASMA MEMBRANES OF HERPES SIMPLEX VIRUS TYPE 1 TRANSFORMED HAMSTER CELLS.

Schneider D, Brauer D, Falke D

(c/o Falke) Inst. Medical Microbiology, Div. Experimental Virology, Johannes Gutenberg-Univ., Hochhaus Augustusplatz, D-6500 Mainz, W. Germany

Biochim Biophys Acta; 685(1):94-104 1982

Plasma membrane extracts from Herpes simplex virus Type 1 transformed hamster embryo fibroblasts were chromatographed on Lens culinaris lectin coupled to Sepharose (LcH-Sepharose) an d analyzed by dodecyl sulfate polyacrylamide gel electrophoresis. Coomassie blue-staining revealed two major protein bands with apparent mol wt of 125,000 and of about 75,000-90,000. In plasma membranes isolated from these tumor cells prior labeled with [3H]fucose or [3H]glucosamine these bands contained the highest amounts of incorporated radioactivity. Separation by LcH-Sepharose-affinity chromatography as well as metabolic labeling clearly demonstrates their glycoprotein character. The 125,000 protein coincides with alkaline phosphodiesterase I activity with a Km of 6.10(-4) M for TMP p-nitrophenyl ester and is competitively inhibited by UDP-N-acetylglucosamine. This enzymatic activity is also present in normal hamster embryo fibroblasts. Gel electrophor-

esis of the Lens culinaris lectin-binding glycoproteins from plasma membranes of normal hamster embryo fibroblasts additionally revealed a strong alkaline phosphatase activity represented by an apparent mol wt of 150,000, while HSV1 hamster tumor cells contain only a very weak activity of this enzyme activity. HSV-lytically infected cells, however, have unchanged levels of alkaline phosphatase activity, whereas alkaline phosphodiesterase activity increases slightly. (Author abstract) (36 Refs)

CLINICAL/ DIAGNOSIS/ IMMUNOTHERAPY

6. EARLY JUDGMENT ON THE RESULTS IN RADIATION THERAPY OF COLORECTAL CANCER: DETERMINATION OF CARCINOEMBRYONIC ANTIGEN (CEA) IN BLOOD SERUM AT DAILY INTERVALS FROM THE BEGINNING OF IRRADIATION.

Pompecki R, Schleusner V, Ziegler HW, Winkler R, Rehpenning W
II. Med. Klinik, UK Eppendorf, Martinistrasse 52, D-2000 Hamburg 20, W. Germany
Strahlentherapie; 157(2):81-85 1981

Carcinoembryonic antigen (CEA) and lactate dehydrogenase (LDH) as tumor cell markers have been determined in the blood serum of 10 patients with colorectal cancer, who underwent preoperative irradiation with 200 to 250 rad daily (total focal dose 2,000 to 2,500 rad). Daily analysis was made during the irradiation, and, moreover, a determination 2 wk after the resection of the tumor. Simultaneously CEA and LDH were determined in 10 controls. Serum CEA and LDH levels were found significantly increased in tumor patients as compared to controls. The course was characterized by a peak of LDH on days 4 and 7 from the onset of radiation treatment, while serum CEA did not show a peak in the total of the tumor patients; but in three individual patients a peak was detected. In five patients, with low CEA values from the beginning, no significant modifications of CEA did appear. Thus, some of the patients undergoing irradiation revealed CEA kinetics conform to theoretical considerations, suggesting a response to irradiation of the colorectal carcinoma. The prognostic value of the early CEA kinetics during radiation treatment should be examined in patients being irradiated for inoperable local recurrence. (Author abstract) (16 Refs) (In GER)

7. PREDICTIVE VALUE OF PLASMA CEA LEVELS: PREOPERATIVE PROGNOSIS AND POSTOPERATIVE MONITORING OF PATIENTS WITH COLORECTAL CARCINOMA.

Szymendera JJ, Nowacki MP, Szawlowski AW, Kaminska JA
Inst. Oncology, P.O. Box 47, PL-00973 Warsaw 22, Poland
Dis Colon Rectum; 25(1):46-52 1982

Plasma CEA levels were determined in 280 patients with histologically proven colorectal carcinoma: in 180 once or twice preoperatively and repeatedly postoperatively, and in 100 postoperative only. Preoperative levels correlated directly with surgical-pathologic state and inversely with the time of recurrence; ie, groups of patients with more advanced stage showed higher proportion of elevated CEA levels, and patients with higher levels had recurrences earlier. Levels above 20 ng/ml were strongly suggestive of liver metastases or disseminated disease. Postoperative plasma CEA levels displayed three patterns of variation. (1) Levels fluctuating within normal range, below 3.2 ng/ml, strongly evidenced that surgery was effective, and (2) those fluctuating below 7.5 ng/ml indicated usually nonmalignant concomitant disease; in either group no more than 10% of the patients had recurrences. (3) Levels rising persistently from a postoperative nadir indicated recurrence or, when the rise was dramatic, liver metastases or disseminated cancer in at least 97% of the patients. (Author abstract) (31 Refs)

8. DEVELOPMENT OF RISK FACTOR PROFILES FOR INDIVIDUALS WITH INCREASED SUSCEPTIBILITY TO CANCER OF THE LARGE INTESTINE.

Lipkin M, Nordlicht N, Nigro ND, Wogan GN, Montesano R, Venitt S, Bruce WR, Archer MC, Wilkins TD
Memorial Sloan-Kettering Cancer Center, New York, NY, 10021
Banbury Rep; 7:97-118 1981

Several populations at high risk of colorectal cancer (CRC) have been registered at Memorial Hospital, including asymptomatic persons and spouses: hereditary polyposis syndromes; site-specific CRC without polyposis; familial multiple cancers inducing CRC; and CRC patients with a second primary malignancy and a family history of CRC, cancer other than CRC, or no cancer. The registry also includes data on families having 41 cancer-free members over at least two generations. In familial CRC, the age at CRC onset differs significantly from the age at CRC onset in the general population. An attempt is being made to identify persons at high risk of CRC who are destined to develop CRC. The phenotypic characteristics collected into the 'risk profile' for patients with familial polyposis include the percentage of 3H-thymidine-labeled epithelial cells in the upper third of the colonic crypts in random biopsy specimens of flat colonic mucosa; the carcinoembryonic antigen content of colonic lavage specimens; mixed lymphocyte reactivity to allogeneic stimuli; the distribution of normal and abnormal actin concentrations in cultured cutaneous fibroblasts; and fecal concentrations of undegraded cholesterol and 7-alpha-dehydroxylase. A systematic analysis of the effects of stress on these parameters has also been started. Other risk factor profiles for other CRC risk groups are being formulated. (39 Refs)

9. CARCINOMA OF THE COLON - PROGNOSIS AND OPERATIVE CHOICE.

Sugarbaker PH
Section Colorectal Surgery, Surgery Branch, NCI, NIH, Bethesda, MD
Curr Probl Surg; 18(12):753-802 1981

Multiple preoperative and intraoperative prognostic variables in patients with colon adenocarcinoma are reviewed. Data from the patient history (diagnosis in the asymptomatic patient, delay in diagnosis, patient age, obstruction and/or perforation as presenting symptoms, hemorrhage as a presenting symptom) and from radiologic, endoscopic, and physical examinations (size, configuration, and location of primary tumor, proportion of circumference of bowel lumen involved, paracolic lymphadenopathy and mobility of rectal cancer by digital rectal examination, colovesical fistula) are discussed. Information from tumor histopathology and preoperative carcinoembryonic antigen determinations is considered. Prognostic data from biopsy of primary tumor is discussed in relation to grading of biopsy specimens (grading systems, correlation of tumor grade and prognosis) and in relation to histologic cell type (mucoid adenocarcinoma, signet ring adenocarcinoma, scirrhous carcinoma). Findings obtained at exploration of the abdomen (enlarged lymph nodes, involvement of adjacent organs or structures) and their impact on survival are discussed. The role of radical colon or rectal excision in treatment of adenocarcinoma is considered. (140 Refs)

10. CLINICAL SIGNIFICANCE OF THE PREOPERATIVE PLASMA CARCINOEMBRYONIC ANTIGEN (CEA) LEVEL IN PATIENTS WITH CARCINOMA OF THE LARGE BOWEL.

Blake KE, Dalbow MH, Concannon JP, Hodgson SE, Brodmerkel GJ, Panahandeh AH, Zimmerman K, Headings JJ
(c/o Concannon), Allegheny General Hosp., 320 East North Ave., Pittsburgh, PA, 15212
Dis Colon Rectum; 25(1):24-32 1982

Preoperative levels of perchloric acid extractable plasma CEA were measured in 911 patients with complaints of the digestive system. A final diagnosis of benign disease was made for 579 patients; 332 patients were found to have cancer. Data for the preoperative CEA values were examined for clinical significance as an aide to diagnosis, preoperative disease staging, and prognosis. The results of our analysis support the conclusions of many investigators that the CEA assay is not a clinically useful diagnostic test, but it shows limited value in preoperative staging and a somewhat stronger correlation with prognosis. (Author abstract) (78 Refs)

11. PANCREATIC ONCOFETAL ANTIGEN IN PANCREATIC JUICES. PARTIAL CHEMICAL CHARACTERIZATION AND DIAGNOSTIC APPLICATION OF A PANCREATIC CANCER-ASSOCIATED ANTIGEN.

Schmiegel WH, Becker WM, Arndt R, Hamann A, Soehendra N, Jessen K, Classen M, Thiele HG
(c/o Thiele) Dept. Clinical Immunology, 1st Medical Univ. Clinic, Martinistrasse 52, 2 Hamburg 20, W. Germany
Scand J Gastroenterol; 16(8):1033-1039 1981

Antisera were raised in rabbits to an antigenic structure present in fetal pancreas tissue, pancreatic tumor tissue, and pancreatic juices and in sera obtained from pancreatic cancer patients. The first chemical data indicate that this pancreatic oncofetal antigen is distinct from CEA, NCA, and NCA2 and is not glycolipid in nature. Immunoelectrophoretic analyses demonstrate that pancreatic oncofetal antigen is a protein or a glycoprotein, which displays microheterogeneity. The apparent mol wt of the basic unit of pancreatic oncofetal antigen is estimated to about 40 K. So far 234 pancreatic juices have been investigated for pancreatic oncofetal antigen. Pancreatic oncofetal antigen was detected within the pancreatic juices from 59 of 74 (80%) pancreatic carcinoma patients but could be traced in only 16%-26% of samples obtained from patients with other diseases. (Author abstract) (21 Refs)

12. ASSOCIATION OF CEA TEST AND LIVER SCAN IN DETECTION OF HEPATIC METASTASES OF GASTROINTESTINAL CARCINOMA.

Buraggi GL, Bombardieri E, Castellani MR, Rodari A, Crippa F
Divisione di Medicina Nucleare, Instituto Nazionale Tumori, Via Venezian 1, 20133 Milan, Italy
Tumori; 67(6):553-558 1981

The authors evaluate the combined use of liver scan and the CEA test in the diagnosis of hepatic metastases of carcinoma of the gastrointestinal tract. Association of the two tests is justified by the fact that the liver scan is very specific but not very sensitive, whereas the CEA test is more sensitive and not very specific. The sensitivity of the CEA test, on the other hand, can be increased by increasing the threshold of normality. However, the associated diagnostic use of the liver scan and the CEA test gives a loss of specificity with respect to the use of the liver scan alone. The present study, carried out on a series of 376 patients affected by gastrointestinal tumors of which 79 were of the stomach (9 with hepatic metastases), 133 of the colon and higher sigmoid (25 with hepatic metastases), and 164 of the lower sigmoid and rectum (29 with hepatic metastases), proposed to establish by use of a statistical method the optimal threshold of the CEA test that would give the best diagnostic specificity of the combined CEA test and liver scan without any relevant loss of sensitivity. A threshold of 26 ng/ml of the CEA test gave a specificity of 92%, a sensitivity of 80%, and an accuracy of 90%. The authors think that in the detect ion of live metastases of gastrointestinal tumors, the combined test can be more helpful the less the probability, for a given patient, for other metastatic localizations. (Author abstract) (26 Refs)

13. ELECTROMYOGRAPHIC EVIDENCE OF INFERIOR GLUTEAL NERVE COMPROMISE: AN EARLY REPRESENTATION OF RECURRENT COLORECTAL CARCINOMA.

LaBan MM, Meerschaert JR, Taylor RS
William Beaumont Hosp., William Beaumont Medical Building, Suite 703, 3535 West 13 Mile Road, Royal Oak, MI, 48072
Arch Phys Med Rehabil; 63(1):33-35 1982

Lumbosacral or primary buttock pain and cutaneous anesthesia in the distribution of the posterior femoral cutaneous nerve were the initial symptoms in five patients later proven to have extensions of previously resected colorectal malignancy. The initial electromyographic impression of an inferior gluteal nerve mononeuropathy associated with recurrent neoplasia was confirmed by a positive colon biopsy in one case and widespread pelvic metastasis demonstrated at laparotomy in the four remaining cases. Four of the five patients also had increased levels of carcinoembryonic antigen. Roentgenographs and other laboratory data were otherwise normal in all five cases. Entrapment of the inferior gluteal nerve and the accompanying posterior femoral cutaneous nerves is facilitated by its medial, intrapelvic fixation at its origin from the sciatic nerve and the crowding effect of the piriformis muscle above, the dorsal rim of the sciatic notch behind and the inferior gluteal vessels and nodes below. The demonstration of hypesthesia over the inferior lateral buttock and a concomitant history of colorectal malignancy should alert the examiner to the possible presence of an inferior gluteal nerve neuropathy. (Author abstract) (7 Refs)

14. CHEMOTHERAPY (ADRIAMYCIN LEVAMISOLE) IN PRIMARY HEPATIC CANCER.

Diaz-Rubio Garcia E, Martin-Jimenez M, Diaz-Rubio Garcia M
Departamento de Medicina Interna, Unidad de Quimioterapia, Facultad de Medicina, Madrid, Spain
Oncologia; 6(6):215-223 1981

Adriamycin (AM) and levamisole (LE) therapy were evaluated in 20 selected patients (13 men, 7 women; 40-80 yr old) with primary hepatic cancer (PHC). Liver cirrhosis was present in 85% of the patients and metastasis (Me) in 30%. Results of test for alpha-fetoprotein were positive in 65% of the patients and results of tests for hepatitis B surface antigen (HbsAg) were positive in 60%. The AM (75 mg/square meter, iv, every 3 wk) and the LE (150 mg/day, 3 days/wk) were administered in at least two cycles. Two patients died during the 1st mo. The reactions to therapy were as follows: 11 progressions, 4 stabilizations, 5 partial remissions, and no complete remissions. The av survival time was 12.5 wk; for the patients with partial remission, the survival time was 32 wk, and for the patients with progression it was only 6 wk. Immunity was studied in 20 healthy controls and in the PHC patients, before the start of therapy and 1 mo later, using the following cutaneous tests: tuberculin, mumps antigen, 2,4-dinitrochlorobenzene (DNCB), and picryl chloride. The results of the tests using tuberculin were positive in two patients before therapy and in seven 1 mo later. All patients were negative to mumps before therapy, but five were positive 1 mo later. Two patients were positive to DNCB before therapy and five after. All patients were negative to picryl chloride before therapy, but four became positive 1 mo later. (46 Refs) (In SPA)

15. A PROSPECTIVE ANALYSIS OF LABORATORY TESTS AND IMAGING STUDIES TO DETECT HEPATIC LESIONS.

Kemeny MM, Sugarbaker PH, Smith TJ, Edwards BK, Shawker T, Vermess M, Jones AE
(c/o Sugarbaker), NIH, Building 10, Room 10N116, Bethesda, MD, 20205
Ann Surg; 195(2):163-167 1982

A prospective study of ability of laboratory tests and liver imaging tests to detect hepatic metastases was performed. Eighty patients at risk for hepatic metastases but without clinical evidence of disease were tested with 13 laboratory tests and 3 liver imaging tests. No single laboratory test had greater than 65% accuracy in the detection of hepatic lesions. No combination of the laboratory tests increased this accuracy. If the laboratory tests were used with one of the liver imaging tests, the accuracy was improved in some combinations to 76%. The CEA assay when analyzed in patients with colorectal primaries had an accuracy of 79%. The results show that the laboratory tests alone are not sufficiently accurate to detect liver metastases. Additional accuracy can be obtained by the combined use of a single liver imaging test and selected laboratory tests. Use of all the liver imaging tests and laboratory tests lowers the accuracy and increases the expense and thus is unnecessary. (Author abstract) (22 Refs)

16. SERUM FERRITIN AND BINDING OF SERUM FERRITIN TO CONCANAVALIN A AS A TUMOR MARKER IN PATIENTS WITH PRIMARY LIVER CELL CANCER AND CHRONIC LIVER DISEASE.

Chapman RW, Bassendine MF, Laulicht M, Gorman A, Thomas HC, Sherlock S, Hoffbrand AV
Dept. Medicine, MRCP, Pond St., London, NW3 2QG, England
Dig Dis Sci; 27(2):111-116 1982

Total ferritin concentration was measured in sera of 30 patients with primary liver cell cancer (PLCC) and 33 patients with cirrhosis and compared with serum alpha-fetoprotein levels as a diagnostic marker of PLCC. Serum ferritin concentration was raised in 19 patients (63%) with PLCC and 11 patients (33%) with cirrhosis. The median level was significantly higher (p less than 0.001) in the PLCC group (560 ug/liter) than in the cirrhotic group (137 ug/liter), although there was considerable overlap. Serum ferritin was positively correlated with serum aminotransferase levels in the cirrhotic patients (r = 0.5 3, p less than 0.001), reflecting hepatic necrosis, but not in the PLCC patients. The concentration of ferritin binding to concanavalin A was measured in the sera of patients with elevated total serum ferritin. Although the proportion of bound ferritin was decreased in the majority of PLCC sera compared to controls (p less than 0.001), there was overlap with the cirrhotic group, making it unlikely that this assay is useful in distinguishing a tumor-specific isoferritin. Serum alpha-fetoprotein levels were elevated in 21 patients (70%) with PLCC and proved to be a highly sensitive and specific test for PLCC. There was no relationship between the alpha-fetoprotein and serum ferritin concentrations. Serum ferritin is inferior to alpha-fetoprotein as an initial screening test for PLCC, but in alpha-fetoprotein-negative patients serum ferritin may have a role in monitoring therapy. Patients with cirrhosis with normal serum alpha-fetoprotein and ferritin concentrations are very unlikely to have PLCC. (Author abstract) (20 Refs)

17. CIRCULATING CEA LEVELS IN PATIENTS WITH FULMINANT HEPATITIS.

George PK, Loewenstein MS, O'Brien MJ, Bronstein B, Koff RS, Zamcheck N
(c/o Zamcheck) Mallory Gastrointestinal Res. Lab., Boston City Hosp., Boston, MA, 02118
Dig Dis Sci; 27(2):139-142 1982

CEA levels were determined in blood specimens from 14 persons suffering from fulminant hepatitis. Values ranged from 1.9 to 21 ng/ml with a mean of 7.0 ng/ml. All except one patient had a CEA level greater than 2.5 ng/ml, but only three exceeded 10 ng/ml. There was no correlation between single CEA levels and prognosis, routine liver chemistries, or histopathologic characterization of hepatic tissue obtained at postmortem examination. These data show that patients with fulminant hepatitis commonly had increased circulating levels of CEA, but these elevations were far less than may be found in patients with hepatic metastases. In severe hepatic dysfunction reduced hepatic clearance of CEA may be responsible for the increased levels. (Author abstract) (19 Refs)

18. SIGNIFICANCE OF PREGNANCY-ASSOCIATED ALPHA2-GLYCOPROTEIN (ALPHA2-PAG) IN PATIENTS WITH BREAST, GASTRIC AND COLORECTAL CANCER.

Shimizu Y, Oshima K, Nakano Y, Fujita M, Taguchi T
Div. Oncologic Surgery, Dept. Clinical Res., Res. Inst. Microbial Diseases, Osaka Univ., 3-1, Yamada-oka, Suita, Osaka 565, Japan
Biken J; 24(3):95-102 1981

Pregnancy-associated alpha2-glycoprotein (alpha2-PAG) levels were measured in human sera by a modification of Laurell's electroimmunoassay using rabbit anti-alpha2-PAG serum. Sera were obtained from healthy controls (32 males and 46 females), patients with benign breast diseases (55 cases), and patients with breast (82 cases), gastric (89 cases), or colorectal (22 cases) cancers. In healthy controls, the mean alpha2-PAG value for females was higher than that for males (p less than 0.05), so alpha2-PAG values for males and females were considered separately in this study. Serum alpha2-PAG levels in patients with benign breast tumors were almost the same as those of controls. In patients with primary breast and gastric cancer, alpha2-PAG levels were higher than those of controls (p less than 0.005) and tended to increase with progress of the disease. Raised alpha2-PAG levels decreased in these patients after curative surgery. These results show that serum alpha2-PAG is useful as a marker in both the initial diagnosis and follow-up of breast and gastric cancer. The reliability of alpha2-PAG as a tumor-associated marker was reinforced by comparison of the positive rates of the three parameters alpha2-PAG, cacinoembryonic antigen (CEA), and immunosuppressive acidic protein (IAP) in patients with breast and gastric cancer. (Author abstract) (22 Refs)

19. AN IMMUNOLOGICAL ASSESSMENT IN PATIENTS WITH UTERINE CERVIX CARCINOMA.

Bonneterre J, Santoro F, Wattre P, Beuscart R, Adenis L, Capron A
Centre Oscar-Lambret, rue Frederic-Combemale, B.P. 307, F 59020 Lille, France
Gynecologie; 32(3):257-266 1981

The relationship between cellular and humoral immunity parameters and stage, treatment and prognosis of cervix cancer was examined in 111 women with carcinoma in situ (12: mean 48.2), Stage I or II neoplasms (57: mean age 52.2), or Stage III or IV neoplasms (42: mean age 62.4). Increased inhibition of phytohemagglutinin (PHA)- or concanavalin A-induced lymphoblastic transformation was evident in more advanced cancers. The percentage and absolute number of T-lymphocytes was identical in the three groups. The percentage of B-lymphocytes was increased in more advanced cancers while the absolute number of B-lymphocytes remained constant. Tuberculin skin tests were positive in 3/7 patients in Group I, 12/32 in Group II, and 8/12 in Group III. Thirty-eight of 93 patients had abnormal levels of circulating immune complexes. The mean plasma carcinoembryonic antigen levels were 8.4, 12.9 and 48.9 nanog/ml for Groups I, II, and III, respectively. No significant difference in IgG and IgM concentrations were observed as a function of group. The mean level of IgA was significantly increased in Group III patients. Complement 3 activity increased with more advanced cancers; complement 4 activity was increased in Group III patients. Various analysis found some associations between clinical and immunological parameters: age of patients, complement factors, and circulating immune complexes; lymphoblastic transformation with mitogens also were closely correlated. Linear regression test demonstrated a relationship between lymphoblastic transformation and skin tests and circulating immune complexes and levels of carcinoembryonic antigen, IgA, IgM, and complement 3. (5 8 Refs) (In FRE)

20. SERUM PROTEINS AND TUMOR MARKERS IN RENAL ARTERIAL AND VENOUS BLOOD IN PATIENTS WITH RENAL CANCER.

Hisazumi H, Nakajima K, Nishino A, Naito K, Kuroda K, Migita S, Konishi K
Dept. Urology, Sch. Medicine, Kanazawa Univ., Kanazawa, Japan
Hinyokika Kiyo; 27(10):1185-1193 1981

In vivo production of some serum proteins and tumor markers in renal cancer tissue, was investigated. Their concentrations in renal arterial and venous blood samples have been determined in 11 patients with renal cancer. In two other groups, one consisting of 13 renal cancer patients without metastasis and another 13 renal cancer patients with metastasis, pre- and post-operative changes of concentration of 36 serum proteins in peripheral blood have been studied as well. The 36 serum proteins were quantitatively determined by a micro-single radial immunodiffusion method described by Migita and five tumor markers, beta-human chorionic gonadotropin (beta-HCG), alpha-fetoprotein (AFP) ferritin, carcinoembryonic antigen (CEA) and beta-2 microglobulin (BMG), were determined using commercially available radioimmunoassay kits. From the data obtained from the 11 patients, it was not possible to assure the production of any serum protein in renal cancerous tissue. A large variety of serum proteins showing a decrease of the concentration in renal venous blood had a relatively close relationship to patients with a large tumor lesion. A sporadic increase of several serum proteins in the venous blood was observed. Production of beta-HCG, BMG and ferritin in renal cancerous tissue was strongly suggested in one, one and five patients, respectively. In the group of 13 patients without metastasis, abnormal levels of Alb, alpha1AT, alpha1AG, Hp, C9 and Hx returned to a normal range after nephrectomy, and these post-operative alpha1AT, alpha1AG, Hp and Hx levels showed a significant difference as compared with post-operative levels of those proteins in the 13 patients with metastasis. These results suggested that post-operative changes of the four serum proteins would be a useful parameter for the occurrence of a deteriorating event in the subsequent course, eg, tumor recurrence or metastasis development. (25 Refs) (In JPN)

21. MEDULLARY CARCINOMA OF THE THYROID. DIAGNOSTIC AND THERAPEUTIC PROBLEMS.

Spreafico G, Colombo L, Puricelli G, Belloni G, Ravetto C
Servizio di Medicina Nucleare, Ospedale Generale Principale di Busto Arsizio, Busto Arsizio, Italy
Recenti Prog Med; 71(3):274-305 1981

Of 700 patients with malignant thyroid cancer observed between 1960 and 1980, 28 (10 men, 18 women; 22-69 yr old) had medullary carcinoma of the thyroid (MCT). Among these MCT patients were four brothers and one sister. The mother had no pathology of the thyroid; the father was dead but, based on radiographic examination had been diagnosed to have had bilateral nodular hyperplasia of the thyroid, with multiple bilateral calcification. One brother had a suprarenal pheochromocytoma (SP) that was removed before resection of the thyroid. The other three had nephrolithiasis; all five siblings had multiple bilateral foci of the MCT. Another patient with the bilateral MCT had thyroidectomy, followed by uncontrollable hypertensive crisis and death 2 days later; at autopsy, two large SP were found. Fourteen patients with monolateral MCT and, when possible their relatives, were examined and had determinations for calcitonin (CT) and carcinoembryonic antigen (CEA), but no familial pathology was noted. Metastases (ME) of lymph nodes were observed in the 15 patients. Cycles of radiotherapy were administered to 22 patients, 10 of whom also received I131. Antiblastic therapy was not used. Of seven patients with multiple endocrine cancers, one died due to bilateral SP 2 days after surgery, one had the ME, the others were well, but four had elevated values of CT and CEA. Of the remaining 21 patients, 17 were living, 11 of whom were without signs of relapse or ME. Problems associated with diagnosis and therapy were discussed. (121 Refs) (In ITA)

22. DIAGNOSIS AND TREATMENT OF LEPTOMENINGEAL METASTASES FROM SOLID TUMORS: EXPERIENCE WITH 90 PATIENTS.

Wasserstrom WR, Glass JP, Posner JB
(c/o Posner), Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
Cancer; 49(4):759-772 1982

The clinical findings and response to treatment of leptomeningeal metastases from solid tumors are analyzed in 90 patients treated at Memorial Sloan-Kettering Cancer Center during the period from January 1975 to February 1980. Patients included those who had either typical clinical findings of leptomeningeal tumor or conclusive laboratory evidence supporting the diagnosis. Carcinoma of the breast (46 patients), lung (23 patients) and melanoma (11 patients) were the common primary tumors. Symptoms of leptomeningeal metastasis occurred as the presenting sign in five patients and as late as 10 yr after the primary tumor was diagnosed in four other patients. Most patients had active systemic disease outside the nervous system. Signs and symptoms could be classified as involving either the brain, cranial nerves, or spinal nerves. Most patients had either symptoms or signs in more than one area at the time the diagnosis was established. The initial spinal fluid examination was abnormal in all but three patients, but only 49 had cytologic evidence of leptomeningeal metastases. Repeated spinal fluid assay yielded a positive cytology in 82 patients. Measurement of biochemical markers, including beta-glucuronidase, carcinoembryonic antigen and lactic dehydrogenase, assisted in the diagnosis. Approx half of the patients treated by intraventricular methotrexate experienced improvement or stabilization of neurological symptoms for more than a mo; median survival was 5.8 mo after diagnosis, with a range of 1-29 mo. In 18 patients disease was limited to the nervous system, and median survival was 8 mo, with four patients surviving 1 yr and two patients for 2 yr. Side effects of therapy were, for the most part, minor. We conclude that vigorous treatment of leptomeningeal metastases with intrathecal chemotherapeutic agents improves symptomatology in some patients, and at times prolongs survival. (Author abstract) (52 Refs)

23. EFFECT OF A CONJUGATE OF DAUNOMYCIN AND ANTIBODIES TO RAT ALPHA-FETOPROTEIN ON THE GROWTH OF ALPHA-FETOPROTEIN-PRODUCING TUMOR CELLS.

Tsukada Y, Bischof WK, Hibi N, Hirai H, Hurwitz E, Sela M

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Proc Natl Acad Sci USA; 79(2):621-625 1982

Daunomycin was covalently attached via a dextran bridge to specific antibodies against rat alpha-fetoprotein produced in a horse. The effect of this conjugate on an alpha-fetoprotein-producing tumor was investigated in terms of cytotoxicity and inhibition or retardation of tumor development. Under the experimental conditions used, the covalent conjugate was by both criteria more efficient than either daunomycin alone or a mixture of daunomycin and specific antibodies or a conjugate of daunomycin with horse immunoglobulin. These results show that the conjugate may be useful as a specific cytotoxic agent against alpha-fetoprotein-producing tumors. (Author abstract) (29 Refs)

24. EMBRYONAL CARCINOMA OF THE TESTICLE IN CHILDREN: REPORT OF 3 CASES.

Pinus J, Braz A, Okuyama MH, Fasano JC, Gulmini LC

Clinica de Cirurgia Pediatrica, Hospital do Servidor Publico Municipal, Sao Paulo, Brazil

Pediatr Mod (Sao Paulo); 16(6):275-278 1981

Three babies (6, 10, and 11 mo old) had surgery because of testicular tumors. Histologic examination indicated testicular embryonal carcinoma. All of the patients were in Stage II. Radiotherapy was administered after surgery in one case. The patients died a few mo after orchiectomy. Determinations of alpha-fetoprotein, luteinizing hormone, and follicle-stmulating hormone were recommended. The inguinal route should be used for surgery, and biopsy in situ must be avoided. (22 Refs) (In POR)

25. AN INTRODUCTION TO CURRENT CONTROVERSIES IN CANCER MANAGEMENT: STAGE I TESTICULAR CANCER--A CASE IN POINT.

Hubbard SM, Macdonald JS

Scientific Information Branch, Div. Cancer Treatment, NCI, NIH, Landow Bldg., Rm. 8C08, 7910 Woodmont Ave., Bethesda, MD, 20814

Cancer Treat Rep; 66(1):1-3 1982

Recent advances in the chemotherapy of advanced testicular tumors, especially cis-Platinum and the synergistic combination of vinblastine and bleomycin, have led to curative treatments. Recurrences can be detected early with marker assays (human chorionic gonadotropin, alpha-fetoprotein, etc), computer-assisted tomography, and ultrasonography. Adjuvant chemotherapy has been accepted for Stage II patients at high risk of relapse after local treatment, and for patients with minimal residual disease. Because minimal disease can be reliably detected in an early stage and even advanced disease can be cured, it may be possible to manage Stage I patients by regular observation (1x/mo) after orchiectomy, giving chemotherapy only if recurrence develops. Those Stage I patients who have been cured by local therapy can thus be spared the toxicity of adjuvant chemotherapy. (16 Refs)

26. SENSITIVE THREE-PARAMETER FLOW-CYTOMETRIC DETECTION OF ABNORMAL CELLS IN HUMAN CERVICAL CANCERS: A PILOT STUDY.

Valet G, Ormerod MG, Warnecke HH, Benker G, Ruhenstroth-Bauer G

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J Cancer Res Clin Oncol; 102(2):177-184 1981

The cell vol, the DNA, and the carcino-embryonic (CEA) or epithelial-membrane (EMA) antigen of formaldehyde-fixed human cervical cells from 21 malignant cervix tumors and 11 normal patients were measured simultaneously with a Fluvo-Metricell flow cytometer. The simultaneous cell vol and DNA measurement provided the distinction of morphologically intact cells from cell debris, the determination of the cell cycle phase combined with the detection of aneuploid cells, and the distinction of inflammatory cells from parenchymal and tumor cells. Malignant samples were recognized because they contained more than 0.5% CEA positive cells which were of intermediate size. CEA and EMA expression in the malignant samples was not linked. The false positive rate in a total of 32 samples was 6.3% when the sum of CEA and EMA positive cells of each cell sample was calculated. No false negative malignant sample was observed. (Author abstract) (26 Refs)

ULTRASTRUCTURE/ CYTOCHEMISTRY

27. CELLULAR LOCALIZATION OF AFP, HCG AND ITS FREE SUBUNITS, AND SP1 IN EMBRYONAL CARCINOMA OF THE TESTIS AND OVARY.

Furumoto M

Dept. Pathology, Kobe Univ., Sch. Medicine, 5,7-Chome, Kusunoki-Cho, Chuoku, Kobe, Japan

Pathol Res Pract; 173(1/2):12-21 1981

An immunohistologic study of AFP, hCG and its free subunits, and SP1 was investigated in 10 cases of non-seminomatous germ cell tumors of the testis and ovary. AFP was demonstrated in mononuclear embryonal tumor cells within embryonal carcinoma in a narrow sense, frequently in association with yolk sac tumor. AFP was more consistently demonstrated in vacuolated or elongated cells of yolk sac tumor, in which continuous transformation from tubular patterns of embryonal carcinoma was shown with positive reactions from AFP. The hCG was demonstrated in syncytiotrophoblastic giant cells scattered among the em bryonal carcinoma, but rarely in mononuclear large cells. The occurrence of hCG and beta subunit was more frequently observed than alpha subunit or SP1, suggesting the unbalanced synthesis of hCG and free subunit in choriocarcinomatous element associated with embryonal carcinoma. These findings support the view that embryonal carcinoma has a developmental potential to the extra-embryonic components of both choriocarcinoma and yolk sac tumor. (Author abstract) (29 Refs)

28. ULTRASTRUCTURAL STUDIES OF XENOGRAFTED HUMAN GERM CELL TUMORS.

Monaghan P, Raghavan D, Neville AM

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Cancer; 49(4):683-697 1982

Xenografts have been established in immune-suppressed mice from three embryonal cell carcinomas, two yolk sac carcinomas, and a 'seminoma-like' tumor that produces alphafetoprotein. The ultrastructural features of these xenografts have been studied in detail and compared with human germ cell tumors removed from patients. A spectrum of ultrastructural differentiation has been demonstrated for tumors of the same histologic classification (embryonal cell carcinoma) and within individual tumors. Cells with ultrastructural appearances intermediate between seminoma and yolk sac carcinoma and between embryonal cell and yolk sac carcinoma have been demonstrated, and their potential implications for tumor histogenesis are discussed. (Author abstract) (29 Refs)

29. TUMOR MARKERS IN INCLUSION CYSTS OF THE OVARY.

Blaustein A, Kaganowicz A, Wells J

Dept. Pathology, Booth Memorial Medical Center, 56-45 Main St., Flushing, NY, 11355

Cancer; 49(4):722-726 1982

The immunoperoxidase method was used to determine whether carcinoembryonic antigen, beta subunit of HCG placental lactogen, pregnancy-associated alpha-2 glycoprotein, and pregnancy-specific beta-1 glycoprotein could be found in inclusion cysts of the ovary. These tumor markers are found in the serum of patients with common epithelial carcinomas of the ovary and inclusion cysts are considered to be the origin of these tumors. Placental lactogen was found in 56 of 118 inclusion cysts, beta subunit of HCG in 4 of 141 cysts, alpha-2 glycoprotein in 5 of 141, and beta-1 glycoprotein in 2 of 118. It was concluded that primitive cells in inclusion cysts elaborate the same tumor markers found in serous cystadenoma and cystadenocarcinoma of the ovary. This observation, although not proving origin of tumor from the inclusion cyst, demonstrates a significant characteristic shared in common by all three. (Author abstract) (15 Refs)

REVIEWS/ OTHER RELATED STUDIES

30. TUMOR MARKERS FOR MALIGNANCIES OF THE DIGESTIVE SYSTEM.

von Kleist S, Hohneck A
Institut fur Immunbiologie, Universitat Freiburg, Stefan-Meier-Strasse 8, D-7800 Freiburg i. Br., W. Germany
Internist (Berlin); 23(1):10-12 1982

The value of serum alpha-fetoprotein and carcinoembryonic antigen (CEA) as markers for tumors of the gastrointestinal tract is discussed. The occurrence of these two markers in patients with benign conditions is noted, and differentiation of benign and malignant diseases through the use of tumor markers is considered. CEA determinations are discussed with respect to two major uses: evaluation of the extent of a tumor at the initial diagnosis, and monitoring of treated patients for early detection of tumor recurrence or metastasis. (6 Refs) (In GER)

31. RECENT DEVELOPMENTS IN THE IMMUNODIAGNOSIS OF CANCER.

Mavligit GM
Dept. Clinical Immunology and Biological Therapy, Univ. Texas M. D. Anderson Hosp. and Tumor Inst., Houston, TX
Cancer Bull; 33(6):250-254 1981

Recent developments in the use of carcinoembryonic antigen (CEA), beta-2-microglobulin, pancreatic carcinoma-associated antigens, prostatic carcinoma-associated markers, miscellaneous tumor-associated antigens, and monoclonal antibodies for immunodiagnosis of cancer are discussed. CEA is useful for early detection of recurrent disease following surgical resection of primary colorectal tumors. The possibility that unnecessary exploratory laparotomies are being performed as a result of more extensive use of serial CEA determinations is discussed; however, serial studies showing a persistent and progressive pattern of rising CEA justify an intensive effort toward tumor localization. Simultaneous determination of beta-2-microglobulin in cerebrospinal fluid and plasma indicates CNS involvement in patients with hematologic malignancies even earlier than the appearance of positive cytology and is used routinely in the total treatment plan of patients with acute leukemia and lymphoma. CEA levels in patients with pancreatic cancer are frequently higher than those in patients with disseminated colorectal cancer. New immunoassays based on pancreatic carcinoma-associated markers are being developed. Radioimmunoassay for prostate acid phosphatase is unlikely to be useful for prostatic carcinoma screening but may be used for more accurate staging. Other tumor-associated antigens include human chorionic gonadotropin, sialoglycoproteins, tissue polypeptide antigen, Tennessee antigen, beta-glucuronidase, and nucleolar antigens. Clinical trials are needed to show whether monoclonal antibodies have any advantage over conventionally prepared antisera in cancer immunodiagnosis. (21 Refs)

32. SERUM TUMOR MARKERS.

Klee GG, Go VL
Section Clinical Chemistry, Mayo Clinic, Rochester, MN, 55905
Mayo Clin Proc; 57(2):129-132 1982

Four tests that currently have wide clinical applications are discussed: carcinoembryonic antigen, human chorionic gonadotropin, alpha-fetoprotein, and prostatic acid phosphatase. Other antigens, proteins, and enzymes have been proposed for the diagnosis and monitoring of malignancy, but most lack sensitivity or are nonspecific. Tumor markers are useful principally in staging or classifying disease and in monitoring the response to treatment. (28 Refs)

33. CLINICAL USEFULNESS OF MARKERS IN MONITORING PATIENTS WITH CANCER.

Pogach LM, Vaitukaitis JL
Section Endocrinology and Metabolism, Thorndike Memorial Lab., Boston City Hosp., Boston, MA
Adv Exp Med Biol; 138:387-403 1982

The most commonly used tumor markers which provide clinical evidence of occult tumors or are used to monitor patients with defined tumors are reviewed. These include carcinoembryonic antigen, alpha-fetoprotein and human chorionic gonadotropin. Paraendocrine syndromes associated with tumors (hypercalcemia, ectopic ACTH syndrome, and syndrome of inappropriate anti-diuretic hormone secretion) are discussed with respect to signs and symptoms and therapy. (55 Refs)

34. ALPHA FETOPROTEIN. A SUMMARY OF CURRENT KNOWLEDGE AND CLINICAL VALUE.

Labadie P
Unite fonctionnelle d'hormonologie, Hopital Pellegrin-Tripode, 33000 Bordeaux, France
Rev Prat; 31(55):4057-4065 1981

The use of alpha fetoprotein (AFP) in the diagnosis and course of certain tumors and infections is reviewed. AFP levels rise to 30-3,000 nanog/ml in the plasma, saliva, and urine of patients with malignant primary hepatomas although there is no correlation between tumor size and AFP levels. Higher AFP levels have also been measured in patients with teratoblastomas, and some tumors of the digestive tract. A rise in AFP levels has not been found to correlate clearly with tumor recurrence or metastases. (4 Refs) (In FRE)

35. THE LATEST LABORATORY TESTS FOR CANCER.

Nichols WS, Nakamura RM
Dept. Pathology, Scripps Clinic and Res. Foundation, La Jolla, CA
Consultant; 21(6):131-134 1981

Screening procedures for cancer involving the use of tumor-associated antigens and endocrine-related, enzyme, virus-associated, and lymphocyte cell markers are described. The most useful tumor-associated antigens are those that have fetal components. Alpha-fetoprotein is an embryo-specific alpha-globulin that exists in healthy fetuses and in most persons with primary hepatic carcinoma. Elevated levels of carcinoembryonic antigen occur in many persons with colorectal cancer. Highest levels of pancreatic oncofetal antigen are found in patients with pancreatic carcinoma. Problems with specificity of tumor-associated antigens are discussed. Human chorionic gonadotropin assays are mainly used to monitor the progress of women who have been treated for hydatidiform mole or choriocarcinoma. An assay for pro-ACTH or ACTH may help distinguish between benign and malignant disease in patients with undiagnosed abnormalities that have been noted on x-ray films of the chest. A radioimmunoassay for calcitonin in the serum is useful in the diagnosis of medullary carcinoma of the thyroid. Plasma gastrin assay is a useful screening test for persons with severe peptic ulcer disease who are suspected of having Zollinger-Ellison syndrome. A thyroglobulin assay may be useful in the diagnosis of thyroid adenocarcinoma. Direct radioimmunoassay for serotonin in the serum or plasma is the test of choice for patients suspected of having carcinoid syndrome. 5-Hydroxyindoleacetic acid also may be used in the diagnosis of carcinoid syndromes. Estrogen receptor assays are useful in planning of therapy for breast cancer. (no Refs)

36. HUMAN PANCREATIC ADENOCARCINOMA: IN VITRO AND IN VIVO MORPHOLOGY OF A NEW TUMOR LINE ESTABLISHED FROM ASCITES.

Chen WH, Horoszewicz JS, Leong SS, Shimano T, Penetrante R, Sanders WH, Berjian R, Douglass HO, Martin EW, Chu TM
(c/o Chu), Roswell Park Memorial Inst., 666 Elm St., Buffalo, NY, 14263
In Vitro; 18(1):24-34 1982

A human pancreatic tumor cell line has been established from the ascites of a patient with histopathologically confirmed adenocarcinoma of the head of the pancreas and maintained for more than 12 mo in the laboratory. Epithelioid tumor cell colonies, which resulted from primary tissue cultures of the ascitic cell component, were mechanically isolated by needle micromanipulation. Tumorigenicity was proven in athymic nude mice. Morphologically the pancreatic tumor epithelial cells grew to confluency with moderately tight adhesion to the culture plastic surface and with free-floating cells in the medium. Upon re-establishment of the tumoral xenograft in tissue culture, the epithelial cells retained their original morphology. Histologically the tumor grown in nude mice exhibited prototypic characteristics of the primary adenocarcinoma in the patient, producing abundant mucin and displaying a broad spectrum of glandular differentiation, which ranged from well to poorly differentiated adenocarcinomas with occasionally localized lymphocytic infiltrations. Furthermore, the tumor expressed carcinoembryonic antigen and human pancreas cancer associated antigen. This tumor line, designated AsPC-1, has been cultured for at least 10 passages in vitro and 3 in vivo. It represents a new model for human pancreatic cancer. (Author abstract) (27 Refs)

37. MOLECULAR BIOLOGY: PROTEINS, POLYPEPTIDES, AMINO ACIDS (CANCERGRAM CB27).

International Cancer Research Data Bank Program Office
NCI, Westwood Building, Room 10A18, Bethesda, MD, 20205
Molecular Biology: Proteins, Polypeptides, Amino Acids (Cancergram) This Title is Available Through National Technical Information Service, Springfield, VA, as NTISUB/PB82-9327:; 1982

Cancergrams are serial monthly publications of International Cancer Research Data Bank (ICRDB) Program of the National Cancer Institute. They are prepared from abstracts of recently published cancer research appearing in CANCERLINE and are available from the National Technical Information Service (NTIS). This CANCERGRAM concerns cancer-related biochemical and physicochemical studies of the synthesis, metabolism, structure and characterization of proteins. This includes absorption and transport of amino acids; the intracellular events in RNA-protein translation; the final assembly of polypeptides and proteins; and the biological transformation, degradation and excretion of proteins and protein end-products. The CANCERGRAM covers structural and functional characterization of major classes of cellular proteins, such as histones and other nuclear proteins, the microsomal system, cytoskeletal and mitotic proteins, and both surface and intracellular membrane proteins. Emphasis is placed on observable differences in these protein properties between normal and tumor cells. Studies of extracellular proteins, plasma proteins, and tumor products are generally excluded, except where they provide insight into the basic processes of protein metabolism. Polyamines are covered in a special category within this CANCERGRAM.

Additional coverage of specific proteins of current research interest is provided in the following CANCERGRAMs: CB01, ONCOFETAL PROTEINS; CB24, HORMONES IN CANCER-RELATED BIOLOGY: Non-Steroid Hormones; CB06, STRUCTURAL AND FUNCTIONAL ASPECTS OF CELL MEMBRANES; CB16, CELL BIOLOGY: Growth Regulation, Differentiation; CB08, IMMUNOBIOLOGY AND CANCER: Antibodies and Humoral Immunity; and CB05, IMMUNOBIOLOGY AND CANCER: Tumor-Associated Antigens. This continuing publication was initiated in 1979.

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ONCOFETAL PROTEINS

SERIES CB01 No. 82/08
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STRUCTURE/ IDENTIFICATION/ CHARACTERIZATION

1. IMMUNOCHEMICAL DIFFERENCES AMONG CARCINOEMBRYONIC ANTIGEN IN TUMOR TISSUES AND RELATED ANTIGENS IN MECONIUM AND ADULT FECES.

Matsuoka Y, Kuroki M, Koga Y, Kuriyama H, Mori T, Kosaki G
First Dept. Biochemistry, Sch. Medicine, Fukuoka Univ., 34 Nanakuma, Nishi-ku, Fukuoka 814-01, Japan
Cancer Res; 42(5):2012-2018 1982

We have isolated carcinoembryonic antigen (CEA)-related antigens from meconium and compared them with those in adult feces. Two CEA-related antigens were detected in meconium [nonspecific cross-reacting antigen 2 (NCA-2) and meconium nonspecific cross-reacting antigen] while four CEA-related antigens were found in adult feces [normal fecal antigen 1, normal fecal antigen 2 (NFA-2), normal fecal cross-reacting antigen, and fecal nonspecific cross-reacting antigen, respectively]. By conventional anti-CEA antisera, NCA-2 in meconium, NFA-2 in adult feces, and CEA in tumor tissues were indistinguishable from each other, but they could be distin-

HE 20

guished by specific antibody preparations against a determinant unique to CEA (CEA-distinctive determinant) or to NFA-2 (NFA-2-distinctive determinant). Neither the CEA-distinctive determinant nor the NFA-2-distinctive determinant was detected on the NCA-2 molecule. No antigenic determinants unique to NCA-2 have been detected with the anti-NCA-2 antisera which we have prepared thus far. The mol wt of purified NCA-2 was estimated to be 150,000 to 170,000 as compared to 160,000 to 170,000 for NFA-2 and 170,000 to 180,000 for CEA. NCA-2 had amino acid and carbohydrate compositions similar to those of CEA and NFA-2. All NFA-2 preparations and about one-half of the CEA preparations were sensitive to Pronase E digestion, which released two antigen fragments from these molecules, but NCA-2 preparations were resistant to such digestion. (Author abstract) (34 Refs)

2. UNFOLDED TRANSFERRIN POLYPEPTIDE CHAIN IS IMMUNOLOGICALLY CROSS-REACTIVE WITH SIMILAR DERIVATIVES OF SERUM ALBUMIN AND ALPHA-FETOPROTEIN.

Pekkala-Flagan A, Ruoslahti E
(c/o Ruoslahti) Cancer Res. Center, La Jolla Cancer Res. Foundation, 2945 Science Park Road, La Jolla, CA, 92037
J Immunol; 128(3):1163-1167 1982

Radioimmunoassays utilizing reduced and carboxymethylated (RC) proteins as antigens reveal a cross-reactivity between alpha-fetoprotein (AFP) and albumin. Similar assays were used to study the relationships of AFP and albumin to other serum proteins. Of the several serum proteins tested, transferrin showed the most similarity with AFP and albumin. There was no cross-reactivity of the native proteins, but antisera prepared against RC-albumin and RC-AFP bound 125I-labeled RC-transferrin at high titers, and antiserum to RC-transferrin bound labeled RC-AFP but not RC albumin. inhibition assays utilizing binding of 125I-RC-AFP or 125I-RC-transferrin to anti-RC-albumin showed that the RC derivatives of AFP, albumin, and transferrin were equally efficient inhibitors, whereas other serum proteins inhibited much less. The serum vitamin D carrier protein (Gc protein) showed intermediate reactivity. The reactivities of the antisera to RC-albumins with RC-transferrin and RC-Gc protein were corroborated by immunostaining of proteins separated by sodium dodecyl sulfate/polyacrylamide gel electrophoresis and transferred to nitrocellulose filters. These antisera stained the bands formed by RC derivatives of albumin, AFP, transferrin, and Gc protein, but not other proteins tested. AFP and albumin are known to have amino acid sequence homology. Our results suggest that transferrin and possibly also Gc protein may be structurally related to AFP and albumin. (Au thor abstract) (29 Refs)

3. MONOCLONAL ANTIBODIES RECOGNIZING TUMOR-ASSOCIATED ANTIGEN OF HUMAN OVARIAN MUCINOUS CYSTADENOCARCINOMAS.

Bhattacharya M, Chatterjee SK, Barlow JJ, Fuji H
Dept. Gynecologic Oncology, Roswell Park Memorial Inst., Buffalo, NY, 14263
Cancer Res; 42(5):1650-1654 1982

Spleen cells from BALB/c mice immunized with human ovarian cystadenocarcinoma extract were fused with the mouse myeloma cell line P3/NSI/1-Ag 4 in the presence of polyethylene glycol (Mr 4,000). Of the 46 hybrids obtained, four secreted antibodies preferentially reactive to the immunizing ovarian tumor extract. Two of these hybrids, which showed no reaction with normal controls, were selected for cloning by the limiting dilution method. The numerous clones obtained from each hybrid were screened against a panel of five ovarian tumor extracts, pooled normal ovary extracts, and pooled normal human sera. One clone from each hybrid that showed specificity for ovarian mucinous cystadenocarcinomas was recloned to assure monoclonality and to establish a permanent hybridoma cell line. The antibodies secreted by these cell lines were of IgG1 subclass with kappa light chains. These antibody-producing hybridomas were selected for further analysis of the antibody specificity by a solid-phase radioimmunoassay and quantitative absorption tests. The antigenic determinant recognized by these monoclonal antibodies was unrelated to carcinoembryonic antigen, normal glycoprotein, normal human serum components, or human ABO blood group materials. These antibodies, which have relatively high affinity and can be produced in large amounts, will be useful for the isolation and immunochemical characterization of this antigen. The purified antigen and the specific antibodies could be then combined in a sensitive radioimmunoassay for the early detection of the antigen in the sera and body fluids of patients with ovarian mucinous cystadenocarcinomas. (21 Refs)

ASSAY PROCEDURES/ SYNTHESIS

4. IMMUNODIAGNOSIS OF HUMAN MELANOMA: CHARACTERIZATION OF HUMAN MELANOMA ANTIGENS AND THEIR DETECTION IN SERA OF MELANOMA PATIENTS BY RADIOIMMUNOASSAY.

Ishii Y, Mavligit GM
Dept. Pathology, Sapporo Medical Coll., S1 W17, Sapporo 060, Japan
Oncology; 39(1):23-28 1982

Double antibody radioimmunoassay (RIA), using radioiodinated melanoma-associated antigens (MAA), rabbit antiserum raised against 3 M KCl extract of human melanoma (AHMS) and goat antirabbit IgG antibody, was employed for the detection of MAA in tumors as well as in sera of melanoma patients. MAA were partially purified from crude KCl extract of melanoma tissue by affinity column chromatography using AHMS and concanavalin A. A high content of MAA was detected in all but one melanoma extract, while normal tissue and nonmelanoma tumor extracts contained MAA to a much lesser extent than did melano ma extracts. MAA were also found in melanoma patients' sera (20/45) but not in sera of normal donors (0/10) and colon cancer patients (0/10). Immunochemical data suggest that AHMS-defined MAA consist of two major glycoproteins with mol wt of 37K and 31K daltons, which does not cross-react either with carcinoembryonic antigen or beta2-microglobulin or with BCG. (Author abstract) (29 Refs)

5. USE OF SANDWICH ENZYME IMMUNOASSAY WITH GLASS BEADS TO DETECT LUNG CANCER CEA AND AFP.

Zhao J, Niu F, Yan Y, Zhou G
Dept. Experimental Immunology, Dongzhimen Hosp., Beijing Coll. Traditional Chinese Medicine, Beijing, People's Republic of China
Chin Med J [Engl]; 94(11):779-784 1981

Levels of carcinoembryonic antigen (CEA) and alpha-fetoprotein (AFP) were determined in sera of 42 patients with bronchogenic carcinoma (BC), 25 with benign lung disorders (BLD), and 46 normal controls using a sandwich enzyme immunoassay with glass beads. The specially-designed glass beads were coated with silicon-NH2 and glutaraldehyde to conjugate purified antibody. In the 46 controls (26-61 yr old) CEA serum values greater than 5 nanog/ml (abnormal) were found in only three males; false positives were found in 6.52%. Serum AFP values were within the normal range in a group of 50 normal subjects. Serum CEA values greater than 5 nanog/ml were found in 29/42 (69%) patients with BC; elevated levels occurred in 11/13 adenocarcinomas, in 12/22 epidermoid carcinomas, and in 6/7 undifferentiated carcinomas. Elevated CEA was found in 8/25 BLD cases and 3/46 normal controls. In lung cancer patients undergoing treatment with Polyporus umbellatus and chemotherapy, the CEA value fell when the tumor regressed and symptoms improved and increased when the tumor enlarged and the patient's clinical condition worsened. AFP values of 30 cases of BC were greater than 20 nanog/ml in only 2 patients, both with bone metastases and elevated CEA values. Determination of serum CEA level may be useful in prognostic assessment of BC patients. (14 Refs)

6. OBSERVATIONS ON RELIABILITY OF COMMERCIAL ASSAY FOR ALPHA-FETOPROTEIN.

Fowler JE

Dept. Urology, Univ. Virginia Medical Center, Box 422, Charlottesville, VA, 22908

Urology; 19(3):275-277 1982

Thirty patients with nonseminomatous germ cell tumors of the testis were monitored with serum levels of alpha-fetoprotein (AFP). Each patient had at least one AFP determination performed in duplicate: one by the National Institutes of Health (NIH) and one by a commercially available assay. With respect to normal and elevated levels, there was agreement in 60 of the 69 duplicate AFP determinations (87%). Six of the 9 discordant AFP determinations were due to increased sensitivity (a lower normal range) of the NIH assay. There was a close correlation between the quantitative levels of AFP when both the NIH and commercial levels were elevated. (Author abstract) (7 Refs)

7. IMMUNOLOGICAL COMPARISON OF OVARIAN AND COLONIC CEA.

Burtin P, Lamerz R, Gendron MC, Maunoury MT, Schnabel G

Institut de Recherches scientifiques sur le Cancer, BP 8-94802 Villejuif, France

Immunol Lett; 4(2):87-91 1982

Carcinoembryonic antigen (CEA) prepared from liver metastases of colon carcinomas (3 samples from 2 different livers) and from the ovary (2 from carcinomas, 2 from benign cysts) were compared immunologically by means of antisera prepared against each of them in rabbits. The Ouchterlony immunodiffusion technique showed the two antisera were identical. Radioimmunological experiments showed slight differences between some, but not all, ovarian and colonic CEAs and between individual preparations of colonic CEA. No organ specificity could be demonstrated for ovarian CEA. Ovarian cancer sera were assayed for CEA using both radioimmunoassay systems: anti-colonic CEA serum and colonic CEA as tracer, and anti-ovarian CEA serum and ovarian CEA as tracer. The values given by the two assays were highly correlated (rs = 0.8107, p less than 0.001), meaning that an organ specific assay for ovarian CEA is not needed. (8 Refs)

8. CARCINOEMBRYONIC ANTIGEN (CEA) EXPRESSION IN SOMATIC CELL HYBRIDS.

Sheer D, Brown RM, Bobrow M

Imperial Cancer Res. Fund, P.O. Box 123, Lincoln's Inn Fields, London WC2A 3PX, England

Somatic Cell Genet; 8(1):1-13 1982

Five intraspecific somatic cell hybrids formed between a human carcinoembryonic antigen (CEA)-producing colonic tumor cell line, LS174T, and a HeLa derivative that does not produce CEA, BU25.CAPR, were investigated for expression of CEA. The viable LSB clones (16, 20, 44, 45, and 46) all contained BU25.CAPR marker chromosomes; the clones all produced substantial CEA but less per cell than LS174T. The number of chromosomes lost in the hybrids compared with parental cells ranged from 3-17. Seven hybrid clones (LSPG) were formed between LS174T and the mouse melanoma cell line, PG19, and 28 hybrid clones (LSR) were formed between LS174T and the mouse kidney adenocarcinoma cell line RAG. The hybrids retained between 4 and 21 human chromosomes, and each human chromosome was represented in at least seven hybrids. Trace amounts of CEA were found in two hybrids, suggesting either repression of CEA production by the mouse genome or production of a structurally abnormal CEA molecule. (29 Refs)

EXPERIMENTS IN ANIMAL SYSTEMS

9. RETARDATION AND PROMOTION OF GROWTH OF SPONTANEOUSLY APPEARING TUMORS USING IMMUNE LYMPHOCYTES PREVIOUSLY EXPOSED TO EMBRYONIC ANTIGENS.

Gorczynski RM, MacRae S
Ontario Cancer Inst., Toronto M4X 1K9, Ontario, Canada
Cancer Res; 42(3):784-790 1982

Spleen lymphocytes taken from mice at various stages of pregnancy or growth of s c syngeneic tumor implants have been examined for their ability to cause cytolysis of embryo fibroblasts in culture or to affect the growth of the transplanted tumor cells in vivo. Activity of different lymphoid populations in affecting tumor growth in vivo was correlated with activity in vitro, whether cytolysis (growth inhibition) or blocking of cytolysis (growth promotion) was considered. The evidence favors an important role for lymphoid responses to embryo-associated antigens in the control of spontaneous tumor growth, although one cannot yet rule out a crucial role for the host milieu rather than, or in addition to, host cellular elements being the important feature of this control process. (Author abstract) (29 Refs)

10. IMMUNOLOGICAL DETECTION OF SPHINGOMYELIN-CARRYING PROTEIN IN TUMORS AND IN EMBRYONAL RAT LIVER.

Diatlovitskaia EV, Sinitsyna EV, Timofeeva NG, Iakimenko EF, Kuprina NI, Bergel'son LD
M. M. Shemiakin Inst. Bioorganic Chemistry, Moscow, USSR
Biokhimiia; 47(1):62-65 1982

The presence of sphingomyelin-carrying protein (SCP) was studied in the cytosol of hepatoma 27, sarcoma 45, Jensen sarcoma, nephroma RA, and in the normal, regenerating, and embryonal rat liver. SCP was assayed by double immunodiffusion technic. SCP was detected in the postmicrosomal supernatant of all tumors tested. SCP was also present in the embryonal liver. SCP was not detected in the normal and regenerating liver, or in the blood of tumor-bearing rats. (16 Refs) (In RUS)

11. EFFECTS OF HEXAMETHYLENE BISACETAMIDE ON ALPHA-FETOPROTEIN, ALBUMIN, AND TRANSFERRIN PRODUCTION BY TWO RAT HEPATOMA CELL LINES.

Hughes EH, Schut HA, Thorgeirsson SS
(c/o Thorgeirsson) Lab. Chemical Pharmacology, DTP, DCT, NCI, NIH, Building 37, Room 5A13, Bethesda, MD, 20205
In Vitro; 18(2):157-164 1982

Alpha-Fetoprotein (AFP), albumin, and transferrin production by two rat hepatoma cell lines, McA-RH 7777 (7777) and McA-RH 8994 (8994), was determined after treatment with hexamethylene bisacetamide (HMBA). Radioimmunoassays were used to determine the levels of both secreted and intracellular AFP, albumin, and transferrin. After treatment with HMBA for a period of 28 to 96 h a threefold increase in AFP secretion by 7777 and a dose related increase in AFP, albumin, and transferrin secretion by 8994 were observed. In contrast, the secretion of albumin and transferrin in 7777 was inhibited by 60 and 40%, respectively, following treatment with HMBA. The intracellular concentrations of AFP in 7777 and AFP, albumin, and transferrin in 8994 were increased by treatment with HMBA indicating that HMBA is able to stimulate the synthesis of these proteins. The intracellular concentration of AFP, albumin, and transferrin in 7777, when expressed as a percentage of the extracellular concentration of these proteins, did not change significantly during HMBA treatment, indicating that the observed decrease in secreted albumin and transferrin by 7777 is due to decreased synthesis. Similarly, in Line 8994, when the intracellular concentration of the three proteins was expressed as percentage of the extracellular concentration, the only significant change observed was an increase in AFP after 72 hr of HMBA (5 mM) treatment. The observed changes in the synthesis of AFP, albumin, and transferrin in both 7777 and 8994 after HMBA treatment were reversible, as judged by the return to control values upon removal of HMBA from the culture medium. Thus, HMBA stimulates synthesis of the oncofetal protein AFP, a result that appears to be independent of the stage of differentiation of the cell. However, its effect on the synthesis of albumin and transferrin are opposite in the two cell lines, suggesting that the regulation of the synthesis of these two proteins is controlled by factors or conditions that are dependent upon the stage of differentiation of the hepatoma cell lines. (33 Refs)

12. ALPHA-FETOPROTEIN FORMATION AND BIOCHEMICAL CHANGES IN RAT LIVER DURING N-DIMETHYLNITROSAMINE-INDUCED CARCINOGENESIS.

Dolezhalova V, Stratil P, Simickova M, Cherni S, Rubenchik BL, Pliss MB, Gorban' GP
Inst. Clinical and Experimental Oncology, Brno, Czechoslovakia
Eksp Onkol; 4(1):51-55 1982

The effects of dimethylnitrosamine (DMNA) on the biosynthesis of alpha-fetoprotein (AFP) and liver metabolism were studied in male Wistar rats. Animals received a diet containing 0.01% DMNA for 20 wk. Extremely low blood levels of AFP were detected on wk 3-4, 25-26, and 35-36 after the initiation of DMNA administration. The low blood level of AFP was correlated with small number of hepatocytes containing AFP. AFP-positive hepatocytes were detected during the first wk after DMNA administration. The number of AFP-containing hepatocytes reached the max 30 wk after the initiation of the experiment, ie during the period of tumor development. The increase of deoxycytidylate deaminase activity was correlated with the increase of the proliferative activity of liver cells. Marked decrease of glucose-6-phosphatase was observed throughout the entire period of DMNA administration. DMNA did not change the rate of glycolysis or the activity of key glycolytic enzymes. (20 Refs) (In RUS)

13. LOCALIZATION OF ALPHAFETOPROTEIN (AFP) IN MURINE TERATOCARCINOMA.

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Biomedicine; 34(3):140-146 1981

Solid tumors with histopathological characteristics of teratocarcinoma (generally presenting the structures of nervous origin) were induced in the mouse by subcutaneous inoculation with mu rine embryonal carcinoma (EC) cells of line PCC4-azal. An indirect immunoperoxidase technique using anti-mouse AFP antibodies was applied for the localization of the protein on paraffin sections of tissue fixed with acetic acid-ethanol. The PCC4-azal EC cells were AFP negative in vitro. In the solid tumors, the immature embryonal or fetal components (ie tubes, or cysts mimicking the development of the neural tube) and the groups of neuroepithelial cells arranged in more or less differentiating structures (pseudotubes, clusters) were AFP positive; on the contrary, cells of the same differentiated neuroepithelial type, but lacking recognizable tissue architecture, were AFP negative. Mature, adult components were AFP negative. Undifferentiated cancer components, whether structured or not, were AFP negative. These results suggest that the intracellular presence of AFP requires a minimum degree of both cell differentiation and tissue organization. (Author abstract) (23 Refs)

14. PLASMA ALPHA-FETOPROTEIN ELEVATION AND MUTAGENICITY OF URINE AS EARLY PREDICTORS OF CARCINOGENICITY IN BENZO(A)PYRENE FED RATS.

Boyd JN, Misslbeck N, Babish JG, Campbell TC, Stoewsand GS
Dept. Food Science and Technology, Cornell Univ., New York State Agricultural Experiment Station, Geneva, NY, 14456
Drug Chem Toxicol; 4(3):197-205 1981

Weanling male Fischer rats were fed on diets containing benzo(a)pyrene (BaP) at (a) 0 or 1,000 ppm or (b) 0, 1, or 100 ppm for 11 wk on diet (a) or 8 wk on diet (b). Some of the animals' diet contained 500 ppm sodium phenobarbital (PB) for the last 5 wk (none getting 1,000 ppm BaP). Cardiac blood was obtained weekly at wk three and assayed for alpha-fetoprotein (AFP). Hepatic slices were obtained at wk six and stained for gamma-glutamyl transpeptidase (GGT) activity. Also at wk six 8-hr urine samples were taken and assayed by the Salmonella/mammalian microsomal test with S typhimurium strain T98. The AFP level was independent of all diets except for notable elevation at wk six in the 1,000 ppm BaP animals. Except for 1,000 ppm BaP animals assay for GGT was independent of other variables. The mutagenesis assay was positive only for the 1,000 ppm BaP animals at wk six with and without activation, and for the 100 ppm BaP with PB animals at wk eight with activation. The AFP and urinary mutagenesis assays were recommended as co-tests for short term carcinogenicity potential evaluation. (12 Refs)

IMMUNOLOGIC INTERACTIONS

15. CIRCULATING IMMUNE COMPLEXES AS MARKERS OF RESPONSE TO CHEMOTHERAPY IN MALIGNANT TERATOMAS AND GESTATIONAL TROPHOBLASTIC TUMOURS.

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Dept. Medical Oncology, Charing Cross Hosp., London WC2, England

Br J Cancer; 45(2):217-222 1982

Concentrations of circulating immune complexes (CIC) were measured serially during chemotherapy of 22 patients with gestational trophoblastic tumors (GTT) and 11 patients with malignant teratoma (MT) by the polyethylene glycol precipitation and C1q solid-phase assays. Results were correlated with tumor response as measured by serum concentrations of human chorionic gonadotrophin (hCG) and alpha-fetoprotein (AFP). CIC concentrations correlated with disease status in the early stages of treatment in 4/22 patients with GTT and 5/11 with MT. CIC assays were less sensitive than hCG and AFP as a monitor of disease, and also less specific, in that eight patients with GTT and five with MT developed raised CIC concentrations during chemotherapy in spite of sustained complete remission. Measurements of CIC concentrations by present methods are neither sufficiently sensitive nor specific to be of clinical value as a tumor marker in GTT and MT, and this casts doubt on their potential value in other malignancies. Attention should be directed to identification of the components of CIC, some of which may be more cancer-specific. (Author abstract) (25 Refs)

16. EFFECT OF LEVAMISOLE TREATMENT ON THE IMMUNOLOGICAL PARAMETERS AND EARLY PATHOLOGICAL PROGRESSION IN PATIENTS WITH CARCINOMA OF THE UTERINE CERVIX.

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Magy Onkol; 26(1):19-25 1982

The effect of levamisole treatment (3 x 50 mg/day on 3 consecutive days at 2-wk intervals) on immunological parameters was studied in 52 women with carcinoma of the uterine cervix compared with 101 patients subjected to conventional therapy only (radiotherapy and surgery) and healthy controls. The immunological changes were evaluated at the end of a 9-mo follow-up period in all patients. Twenty-five of the 52 levamisole-treated patients and 43/101 conventionally treated patients were clinically tumor-free at the time of evaluation. The carcinoembryonic antigen levels were below 5 nanog/ml in 15/25 and 24/43 tumor-free patients, respectively. Nine patients in the levamisole group and 18 in the conventional therapy group developed recurrences. The immunological tests of the clinically tumor-free patients showed higher alpha-2-macroglobulin levels and lower values of the phytohemagglutinin skin test in the conventionally treated patients than in the levamisole-treated ones. The IgM levels were reduced significantly in both patient groups compared with the controls, but the decrease relative to the control and the initial values was lower in the levamisole group than in the conventionally treated patients. (16 Refs) (In HUN)

17. CELLULAR AND GENETIC RESTRICTIONS IN THE IMMUNOREGULATORY ACTIVITY OF ALPHA-FETOPROTEIN. III. ROLE OF THE MLC-STIMULATING CELL POPULATION IN ALPHA-FETOPROTEIN-INDUCED SUPPRESSION OF T CELL-MEDIATED CYTOTOXICITY.

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J Immunol; 128(3):1134-1140 1982

Alpha-fetoprotein (AFP), a normal component of fetal and newborn sera, exerts selective suppressive effects on various functions of thymus-derived (T) lymphocytes, including the T cell-mediated cytotoxic reaction. In the present study, AFP-induced suppression of the T cell-mediated allogeneic response was examined to define more precisely the mechanism by which AFP acts. Data presented indicate that AFP elicits its effect within the first 24 to 36 hr of culture. However, AFP apparently has no direct effect on T lymphocytes. T cells incubated in the presence of AFP retain full capacity to respond in MLC and CML. In contrast, AFP induces major changes in the functional status of monocyte-enriched, MLC-stimulating cell populations. This monocyte-enriched population, after pretreatment with AFP, possesses strong stimulating capacity for the T suppressor cell limb of the immune response, while at the same time, suppresses the activity leading to the normal generation of cytotoxic T lymphocytes. These data correlate with the immune activity present in the newborn mouse. (Author abstract) (29 Refs)

CLINICAL/ DIAGNOSIS/ IMMUNOTHERAPY

18. USE OF RADIOLABELED MONOCLONAL ANTI-CEA ANTIBODIES FOR THE DETECTION OF HUMAN CARCINOMAS BY EXTERNAL PHOTOSCANNING AND TOMOSCINTIGRAPHY.

Mach JP, Buchegger F, Forni M, Ritschard J, Berche C, Lumbroso JD, Schreyer M, Girardet C, Accola RS, Carrel S

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Immunol Today; 2(12):239-248 1981

Data on Paul Ehrlich's concept of the 'magic bullet' via the use of radiolabeled antibodies as tracers for tumor localization are presented. The first successful detection of carcinoma by external scanning in patients injected with purified 131I labeled anti-carcinoembryonic antigen (CEA) antibodies was reported in 1978. Scanning performed 48 hr after injection detected almost all the CEA producing tumors. In current clinical studies, patients were selected who were scheduled for tumor resection. They were injected simultaneously with 1 mg of goat anti-CEA antibodies labeled with 1 mCi of 131I and the same amount of normal goat IgG labeled with 0.2 mCi of 125I. Using this paired labelling methods, specific uptake of antibodies in tumors was up to 5 times higher than that of control normal IgG. Three possible ways to improve the sensitivity and specificity of immunoscintigraphy as a technique for tumor localization were discussed: (1) use of antibody fragments, (2) use of monoclonal antibodies against CEA, and (3) use of tomoscintigraphy to detect radioactivity localized in the tumor. (26 Refs)

19. DIAGNOSIS AND TREATMENT OF HEPATIC METASTASES OF COLO-RECTAL NEOPLASMS.

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Service de Chirurgie, Institut Jules Bordet, Bruxelles, Belgium
Rev Med Brux; 3(1):29-35 1982

Diagnosis and treatment of hepatic metastases are discussed. Clinical symptoms, such as jaundice, hepatomegaly, palpable liver masses, and ascites, are present only in the later stages of liver tumor development. Alkaline phosphatase is the most commonly measured enzyme for the evaluation of liver metastases. Liver enzymes are of little diagnostic importance since abnormalities may reflect benign or malignant disorders. Carcinoembryonic antigen levels, although not specific for liver metastases, may be useful in the diagnosis of recurrence. Scintigraphy is the classic examination for liver metastases. Echography and tomodensitometry may also be useful in the evaluation of liver tumors while arteriography is of little value. Histologic evaluation may involve percutaneous needle biopsy, laparoscopy, or laparotomy. Surgical treatment is useful only in the presence of a single metastasis or if many metastases are localized in a single liver lobe. The antimitotic agent most commonly used to treat liver metastases is 5-fluorouracil (5FU). Only the combination of 5FU with semustine has produced responses superior to those resulting from 5FU alone. Radiotherapy is of little use in the treatment of liver metastases. Locoregional treatments of liver metastases, including ligature of the hepatic artery and regional chemotherapy (liver arterial perfusion, portal perfusion, arterial perfusion after ligature of hepatic artery, portal perfusion after ligature of hepatic artery) are described. (31 Refs) (In FRE)

20. RADIONUCLIDE AND ROENTGENOLOGICAL DIAGNOSIS OF METASTATIC TUMORS OF THE GASTROINTESTINAL TRACT.

Makeev AI, Ostrovtsev IV, Roshchin EM
Lab. Radioisotope Diagnosis, All-Union Cancer Res. Center, Moscow, USSR
Med Radiol (Mosk); 27(2):45-49 1982

Diagnostic efficacy of computer tomography (CT), scintigraphy with colloid 198Au, 99mTc, and 113mIn, and in vitro radioimmunoassay of the blood levels of carcinoembryonal antigen (CEA) and alpha-fetoprotein (AFP) was evaluated in 161 patients with stomach cancer and in 9 patients with colorectal cancer. Significant increase of the blood level of CEA was observed in all cancer patients (19.5, 39.7, and 84.9 ug/liter in Stages I-II, III, and IV, respectively, compared with 6.4 ug/liter in healthy controls). Significant increase of AFP level was observed only in the patients with advanced Stage III-IV tumors. The increase of CEA level depended upon the size of liver metastases and the size of the primary tumor. AFP level did not depend upon the extent of liver involvement. These findings indicate that CEA assay in combination with CT and scintigraphy can improve diagnosis of liver metastases. (6 Refs) (In RUS)

21. GASTROINTESTINAL TUMORS: PROGNOSTIC FACTORS AND THE STATUS OF CHEMOTHERAPY.

Joss R, Goldhirsch A, Tschopp L, Brunner K
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Dtsch Med Wochenschr; 106(49):1664-1669 1981

Prognosis and status of chemotherapy for gastrointestinal (GI) tumors are reviewed. Results of current methods of treating GI tumors have been unsatisfactory because of generally late diagnosis, poor response to chemotherapy (CT) or radiotherapy (RT), the difficulty of determining the results of treatment, and the small number of cytostatic drugs available. Colorectal cancers (CR) are the most common cancers in industrialized nations. CR occur most frequently in older patients. The 5-yr mortality rate after curative surgery is 50-60%. Factors affecting prognosis include tumor stage, location of metastases, patient age, sex, activity index, grade of malignancy, preoperative carcinoembryonic antigen titer, and duration of disease-free interval. Patients with lung metastases respond poorly to CT but have a favorable prognosis for survival time. The 5-yr survival rate (5ysr) is lower for rectal carcinoma (25%) than for colon carcinoma (32%). The most effective CT agent against CR is 5-fluorouracil (5-FU: response rate 21%). Pancreatic carcinoma (PC) is increasing in incidence. Only 10-15% of all cases are operable. The 5ysr is 5%. CT with 5-FU, adriamycin (ADM), and mitomycin (MM) is recommended for younger patients in good general condition. Combined RT and CT with 5-FU is recommended for inoperable cases. The 5ysr for stomach cancer (SC) is 5-15%. The most important prognostic factor for SC is lymph node involvement. Combination CT with 5-FU, ADM, and MM is recommended for SC. (49 Refs) (In GER)

22. SERUM-ALPHA1-FETOPROTEIN AND SERUM FERRITIN IN LIVER TUMORS.

Polterauer P, Linkesch W
II. Universitatsklinik fur Gastroenterologie und Hepatologie, Garnisongasse 13, A-1090 Wien, Austria
Wien Klin Wochenschr; 94(4):105-108 1982

Values of serum ferritin (SF) were evaluated in 22 patients (16 men, 6 women; 24-78 yr old) with histologically confirmed primary hepatic cancer (PHC); 11 patients had malignant hepatoma (MH) in liver without cirrhosis, 11 had MH associated with different hepatic pathologies; and in 25 patients (13 men, 12 women; 35-78 yr old) with histologically confirmed hepatic metastases (HM) from different primary cancers (12 large intestine, 5 pancreas, 3 stomach, and others). Radioimmunoassay was used for determination of alpha-1-fetoprotein (AFT) with normal values up to 9 nanog (ng)/ml. Heterologous antibody system was used for the determination of SF with the normal values 29-343 ng/ml (measured on 396 healthy controls). AFP values were elevated in 95.4% of PHC patients, but only 81.8% had values greater than 174 ng/ml, which were considered suspicious for PHC. SF values were elevated in 77.2% of PHC patients. Four of PHC patients had increased values of SF, although AFT values were low. SF values were elevated in 88% of HM patients, while AFT values were elevated only in 28%. Using both tests (SF and AFP) diagnosis of hepatic cancer would be increased. Elevated values for SF cannot differentiate between PHC and HM. (19 Refs) (In GER)

23. PRIMARY LIVER CARCINOMA IN CHONGQING.

Liu W, Yuan A, Jin H, Hong D, Luo Y, Zhao S
Dept. Internal Medicine, Affiliated First Hosp., Chinese PLA Third Military Medical Coll., People's Republic of China
Zhonghua Neike Zazhi; 20(7):392-396 1981

Results of a mass-screening and follow-up study are described for primary liver cancer in Chongqing. A higher incidence of liver cancer was found to be associated with males 50 and 60 yr old, history of liver diseases such as hepatitis B, high levels of alpha-fetoprotein, and a positive test for hepatitis B surface antigens. Based on these findings, the importance of the follow-up of high-risk individuals and the early diagnosis of liver cancer is stressed. (3 Refs) (In CHI)

24. ASPECTS OF RESEARCH STUDIES ON LIVER CARCINOMA.

Zhen Y
Shanghai Inst. Cell Biology, Academia Sinica, Shanghai, People's Republic of China
Cancer Research in the People's Republic of China and the United States of America: Epidemiology, Causation and New Approaches to Therapy, Proceedings of a Conference held in New York, 28-29, March, 1980. Marks PA, ed. New York, Grune and Stratton, 273 pp., 1981.

Studies with human liver carcinoma (HLC) and rat hepatoma are summarized. In vitro cultured HLC cell lines, fetal antigens in HLC, localization of surface and core antigen of hepatitis B virus in human hepatoma, cell-mediated cytotoxicity and immune RNA studies in human hepatoma, and experimental hepatoma research are discussed. A transplantable rat hepatoma was established by feeding Wistar rats with diethylnitrosamine in drinking water. The hepatoma exhibited fetal characteristics, including alpha-fetoprotein production, fetal isozyme expression, and the presence of membrane-associated fetal antigen. Research using these model systems and liver material derived from animals during carcinogenesis and from regenerated and fetal livers is described. (19 Refs)

25. ALPHA1-FETOPROTEIN AND TENNESSEE ANTIGEN IN HEPATOCELLULAR CARCINOMAS AND IN METASTATIC LIVER CANCER.

Polterauer P, Muller M
II. Universitatsklinik fur Gastroenterologie und Hepatologie, Garnisongasse 13, A-1090 Wien, Austria
Wien Klin Wochenschr; 94(4):102-105 1982

Alpha-1-fetoprotein (AFP) and Tennessee antigen (TA) were evaluated in sera of 23 patients (15 men, 8 women; 24-78 yr old) with histologically confirmed hepatic carcinoma [15 had malignant hepatomas (MH) in liver free of cirrhosis, 3 had MH associated with alcoholism, 2 had MH after hepatitis, 1 each had MH associated with hemochromatic liver, cryptogenic liver cirrhosis, and chronic aggressive hepatitis], and 20 patients (10 men, 10 women; 35-78 yr old) with histologically confirmed hepatic metastases (HM) from primary cancers (12 colorectal, 2 gastric, 2 salivary gland, 1 each pulmonary, mammary, bladder, and thyroid). Radioimmunoassay was used for determination of AFP with normal values up to 9 nanog (ng)/ml, suspicious for MH greater than 174 ng/ml, and diagnostic for MH greater than 6074 ng/ml. Inhibition of hemoagglutination was used for measuring the TA with normal values up to 7.7 units/ml. AFT values were elevated in 87% of the patients with MH and 65% had values that were suspicious for MH. TA values were elevated in 87% of the patients with MH, but the TA values were in normal range in 85% of the patients with HM. (7 Refs) (In GER)

26. HEPATIC ADENOMA ASSOCIATED WITH ORAL CONTRACEPTIVES.

Woodyer AB
St. James's Hosp., London, England
J R Coll Surg Edinb; 27(1):59-60 1982

Hepatic adenoma associated with oral contraceptives was diagnosed in a 26-yr-old West Indian girl who presented with a 5-yr history of increasingly severe and frequent right hypochondrial pain. The serum alphafetoprotein concentration was 25 ug/liter and an ultrasound liver scan showed a solid mass arising from the lateral portion of the left lobe, well circumscribed, displacing the porta hepatis and gallbladder laterally and with an echo pattern similar to that of normal liver. The tumor was excised with a wedge of normal liver tissue. At follow-up 18 mo after operation no further abdominal pain and no sign of tumor recurrence was reported. (4 Refs)

27. CASE OF HEPATIC CANCER EXHIBITING FREQUENT HYPOGLYCEMIA AND REVIEW OF 91 CASES REPORTED IN JAPAN.

Shio H, Ueki J, Tominaga M
Dept. Internal Medicine, Tottori Prefectural Central Hosp., Tottori, Japan
Nippon Rinsho; 39(10):3342-3348 1981

An autopsy case of hepatic cancer accompanied by hypoglycemia was reported. The patient, a 71-yr-old man, had had a 14-yr history of diabetes. When diagnosed, the diabetes was controlled fairly well with po drugs to reduce blood sugar. The patient presented with general malaise, micturition, and mouth dryness. Presence of alpha-fetoprotein (from 40-600 ug/ml) suggested the existence of hepatic cancer; no clear evidence of tumor was revealed with other tests. Prior to death, despite discontinuation of the blood sugar reducing drugs, hypoglycemia persisted, so the patient was given continuous iv glucose. Examination of autopsy specimens showed a highly-differentiated hepatic carcinoma (Edmondson Type II). Review of 91 cases of hepatic cancer accompanied by hypoglycemia showed that the majority of patients were 40-70 yr old and tumors averaged 3,293 g in men and 3,400 g in women. (38 Refs) (In JPN)

28. SPONTANEOUS REGRESSION OF HEPATOCELLULAR CARCINOMA.

Gottfried EB, Steller R, Paronetto F, Lieber CS
(c/o Lieber) Alcohol Res. Treatment Center, Veterans Admin. Medical Center, 130 West Kingsbridge Road, Bronx, NY, 10468
Gastroenterology; 82(4):770-774 1982

A 65-yr-old alcoholic man developed jaundice and biopsy-proven multicentric hepatocellular carcinoma. Coinciding with abstention from alcohol and without treatment, jaundice has resolved, alpha-fetoprotein has become normal, and there is no evidence of tumor demonstrable by radionuclide scanning or laparoscopic liver biopsy. The patient is alive and well 48 mo after the initial diagnosis. Regression of this tumor in the untreated adult has not previously been reported. (Author abstract) (24 Refs)

29. FACTORS INFLUENCING PRIMARY LIVER CANCER RESECTION SURVIVAL RATE.

Tang Z, Yu Y, Zhou X, Chen Q
Liver Cancer Res. Unit, Zhongshan Hosp., Shanghai, People's Republic of China
Chin Med J [Engl]; 94(11):749-754 1981

Factors affecting survival of 153 patients with surgically treated primary liver cancer were investigated. Of these patients, 24.2% were mass screening patients and 20.3% were subclinical patients. Resection of the right side was performed in 34%, left side in 52.9%, partial in 13.1%, radical in 45.1%, and palliative in 54.9%. Operative mortality rate was 12.4%. Single factor analysis demonstrated 5-yr survival rates of 64.9% in patients with postoperative alpha-fetoprotein (AFP) of no more than 20 nanog/ml compared with 0% in those with greater than 20 nanog/ml; 51% for those treated with radical resection compared with 0% for those treated palliatively; 55.5% for mass survey patients compared with 22.3% for clinical patients; 45.0% for patients with single nodules compared with 4.8% for those with multiple nodules; and 44.4% for patients with preoperative negative AFP agar gel diffusion values compared with 15.3% in those with positive values. Combined analysis of multiple variables demonstrated a better prognosis for patients with countercurrent immunoelectrophoresis values of AFP converting to negative postoperatively, AFP less than 20 nanog/ml postoperatively, tumor no more than 5 cm, radical resection, mass screening, and no symptoms of primary liver carcinoma. The most important factors were normalization of AFP values postoperatively and radical resection. (16 Refs)

30. A SIMULTANEOUS STUDY OF FIVE MARKERS IN 80 CASES OF BREAST CANCER. CARCINO-EMBRYONIC ANTIGEN (CEA), FERRITIN BETA2, MICROGLOBULIN, (BETA M), SUB-UNIT BETA OF CHORIONIC GONADOTROPHIN HORMONE (BETA CGH) AND ALPHA FETOPROTEIN (AFP).

Fourrier E, Kadouche J, Mignot L, Reynier J, Gorins A, Rochet Y, Trevoux R, Gavel M
Centre des Maladies du Sein, Hopital Saint-Louis, 38, rue Bichat, F 75010 Paris, France
Gynecologie; 32(4/5):385-390 1981

Pathological levels of CEA, ferritin (FT), microglobulin (beta M), (CGH), and alpha fetoprotein (AFP) were compared in various stages of breast cancer (80 cases). When the pathologic level of CEA was set at 2.5 nanograms (nanog)/ml, there were positive results in 63% of the cases at diagnosis, 95% of the metastasized cancers, and 42% of the postoperative cases. When the pathologic level of CEA was set at 4 nanog/ml, the percentages of positive cases were 35%, 91%, and 35% respectively. In all cases, the highest positive values were obtained with CEA and FT. The value of beta M was more limited, and CGH and AFP provided very little information. In 18 metastasized cases which were treated with chemotherapy, CEA assays evolved along parallel lines with the clinical course of the disease in 16 cases and in 2 cases, levels of CEA increased while the disease seemed stable. FT evolved along clinical lines in 17 cases, but levels increased in 1 case which seemed to be in regression. The other assay results did not correlate in any significant way with clinical course of the disease. Based on the results of this study, it is recommended that CEA and FT be used to monitor the progress of patients who have been surgically treated for breast cancer and are undergoing adjvant therapy. (15 Refs) (In FRE)

31. POSTOPERATIVE PROCEDURE IN PATIENTS WITH MAMMARY CANCER ACCORDING TO THE PROTOCOL OF THE CENTER FOR ONCOLOGY AND RADIOTHERAPY.

Stula N, Konstantinovic M, Dubravcic M, Perkovic M
Centar za onkologiju i radioterapiju, Opca Bolnica, Split, Yugoslavia
Libri Oncol; 10(2/3):185-188 1981

Patients with mammary cancer (MC) underwent surgery followed by radiotherapy (RT) of the regional lymph nodes. High risk patients were castrated and received adjuvant chemotherapy (CT). Results of the following tests were considered important in chosing the proper therapeutic procedure: carcinoembryonic antigen, lactic acid dehydrogenase, phosphohexose isomerase, and gamma-glutamyl-transpeptidase. Adjuvant CT consisted of methotrexate [40 mg/square meter (m2), days 1 and 3], 5-fluorouracil (600 mg/m2, days 2 and 4), endoxan (300 mg/m2 iv, days 1, 2, 3, 4, 5). Cycles were repeated 5 wk after the start until 6 cycles were adminstered. Palliative procedure used CT according to Cooper: adriablastine after first relapse, and alkeran after the second. Mortality due to MC will decrease, if primary tumor is diagnosed a few yr earlier or if the patients at the time of diagnosis are treated as if they had already metastases. It was suggested that adjuvant CT should become part of primary treatment for MC. (6 Refs) (In SCR)

32. QUANTITATION OF RESPONSE TO THERAPY IN PATIENTS WITH METASTATIC BREAST CARCINOMA BY SERIAL ANALYSIS OF PLASMA GROSS CYSTIC DISEASE FLUID PROTEIN AND CARCINOEMBRYONIC ANTIGEN.

Silva JS, Leight GS, Haagensen DE, Tallos PB, Cox EB, Dilley WG, Wells SA
Sloan-Kettering Memorial Cancer Center, 1275 York Ave., New York, NY, 10021
Cancer; 49(6):1236-1242 1982

The maximum percent change (MPC) of plasma carcinoembryonic antigen (CEA) and gross cystic disease fluid protein (CDP) were correlated with response to therapy in 92 metastatic breast carcinoma patients. In patients treated with hormone therapy MPC values were significantly different between patients with disease progression (Prog) and regression (Reg): MPC-CEA for Reg = 72 +-7%, for Prog = 396 +-150%; MPC-CDP for Reg =-86 +-6%, for Prog = 702 +-330%, p less than 0.001 in a one-way ANOVA for CEA and CDP. Similar differences were noted in patients treated with chemotherapy. Decreased (greater than 50%) plasma CEA levels were observed in 24/29 (83%) of Reg, 18/35 (51%) stable and 0/49 (0%) of Prog; decreased (greater than 50%) plasma CDP levels were noted in 19/24 (79%) of Reg, 21/28 (75%) of stable and 2/35 (6%) of Prog. Patients with plasma marker decreases greater than 50% had significantly longer responses to therapy (14.2 mo for CEA, 14.1 mo for CDP) compared to patients with less than 20% decrease (2.0 mo for CEA, 0.8 mo for CDP), p less than 0.001 in a one-way ANOVA. Decreasing marker levels during the initial 6 wk of therapy (negative slope) accurately identified Reg or stable patients: the predictive value of a negative slope was 92% for CEA and 86% for CDP. Rising marker values correctly identified treatment failures (Prog): the predictive value of a positive slope was 90% for CEA and 76% for CDP. These data indicated that changes in plasma CEA and CDP levels reflected increasing or decreasing tumor burden during hormone or chemotherapy treatment of metastatic breast carcinoma. Criteria have been established to predict therapeutic outcome based on the slope of CEA or CDP after 6 wk of treatment. (Author abstract) (25 Refs)

33. THE PROTOCOL FOR LONG-TERM FOLLOW-UP OF TREATED OVARIAN CANCERS. COELIOSCOPY AND CARCINO-EMBRYONIC ANTIGEN ASSAY.

Bernard P, Kac D, Boury-Heyler, Rochet Y
Service de Gynecologie, Pavillon Paul-Gerin, CHU de Grenoble, BP 217 X, F 38043 Grenoble, France
Gynecologie; 32(4/5):379-384 1981

Coelioscopy is recommended as an excellent follow-up method for patients who underwent treatment for ovarian cancer because it allows a direct vision of the pelvic, digestive, and peritoneal cavities. Areas of peritoneal granulations may be recognized. These granulation areas may then be biopsied, and cytologic examination of cells acquired through peritoneal lavage with physiologic serum may be carried out. Extreme care in the technique used for the examination is recommended because of the high risk of digestive trauma. Coelioscopy is usually carried out 2x a yr but frequency of the examination is in fact dictated by the levels of carcinoembryonic antigen (CEA) should be prescribed for 5 yr following surgery. CEA levels are elevated in 73% of the women who have had ovarian cancer. A level higher than 15 nanog/ml is considered pathologic. The two cases presented demonstrate the importance of close follow-up. In one case, exploratory laparotomy revealed an intraclinical recurrence limited to a single peritoneal metastasis. In the other case. Positive cytology obtained through normal coelioscopic examinations led to further chemotherapy and exploratory laparotomies. (8 Refs) (In FRE)

34. CARCINOEMBRYONIC ANTIGEN IN CASES OF CERVICAL CARCINOMA.

Weppelmann B, Schulz BO, Oberheuser F
Jewish Hosp., Burnett Ave., Cincinnati, OH, 45229
Zentralbl Gynaekol; 103(21):1273-1279 1981

Carcinoembryonic antigen (CEA) was determined by means of solid-phase radioimmunoassay through 1 yr in 83 patients with Groups I through IV cervical carcinoma. The intention was to test CEA diagnosis for its value as a tumor marker in therapeutic monitoring and detection of recurrences. CEA values prior to treatment were above normal, that is in excess of 2.5 ng/ml, in 42.8% of the cervical carcinoma patients. CEA values declined during therapeutic radium and cobalt60 irradiation in 81% of those patients in whom original values had been increased to more than 2.5 ng/ml. No substantive change was recordable from those patients in whom original values had been below 2.5 ng/ml. Recurrence diagnosis gave good agreement between CEA levels and clinical findings in 58% of the cases, falsely negative data in 37% and falsely positive values in 4%. The development of recurrence was repeately sensed by means of CEA determination up to 6 mo before clinical manifestation in 72 patients who had been under long-time monitoring. The usefulness of CEA determination in therapeutic monitoring and after-care of patients with cervical carcinoma was found to be limited to the effect that only increased values were of clinical relevance, whereas no conclusions whatever could be drawn from low values. (Author abstract) (21 Refs) (In GER)

35. PROGNOSTIC FACTORS IN CLINICAL STAGE I NON-SEMINOMATOUS GERM-CELL TUMOURS OF THE TESTIS.

Raghavan D, Peckham MJ, Heyderman E, Tobias JS, Austin DE
(c/o Peckham), Royal Marsden Hosp., Downs Road, Sutton, Surrey SM2 5PT, England
Br J Cancer; 45(2):167-173 1982

Prognostic factors have been studied in 59 men with clinical Stage I non-seminomatous germ-cell tumors of the testis seen at the Royal Marsden Hospital between 1973 and 1978. Fourteen of the patients relapsed, and 45 have remained continuously disease-free. Two factors were identified which showed a significant correlation with relapse following radiotherapy: local extent of the primary tumor, and rate of decline of serum alpha-fetoprotein (AFP) and beta-human chorionic gonadotrophin (hCG) levels following orchidectomy. High serum marker levels at the time of referral after orchidectomy were not prognostically significant per se. The presence of tissue-associated hCG in the primary tumor was not prognostically significant. The results were compared with histology and pathological stage of the primary tumor in patients presenting with lung metastases but no clinical evidence of lymph-node disease. Embryonal carcinoma was more commonly associated with a locally invasive primary tumor and with extralymphatic spread than was teratocarcinoma. (Author abstract) (9 Refs)

36. THE SIGNIFICANCE OF THE TUMOR MARKERS ALPHA-FETOPROTEIN AND BETA-HCG IN STAGING AND MONITORING OF THE COURSE OF NON-SEMINOMATOUS TESTICULAR TUMORS.

Scheulen ME, Pfeiffer R, Kropfl D, Schmidt CG
Innere Universitatsklinik und Poliklinik (Tumorforschung), Westdeutsches Tumorzentrum Essen, Hufelandstrasse 55, 4300 Essen 1, W. Germany
Therapiewoche; 32(5):525-531 1982

The presence of the tumor markers alpha1-fetoprotein (AFP) and beta-human chorionic gonadotropin (b-HCG) was measured regularly in serum of 277 patients with non-seminomatous tumors (NSTT) of the testicle at diagnosis and during the course of the disease. Among 230 evaluable patients at diagnosis AFP was detected in 58% and b-HCG in 53%. At least one of the markers was detected in 77% of the patients. Significant differences in serum levels of b-HCG and lactate dehydrogenase were found between patients in Stages I and IIA and those with more advanced disease. Comparison of serum marker levels before and after radical orchiectomy and retroperitoneal lymph node dissection required reclassification of 10/63 patients with Stage I or II tumors to higher stages. Marker levels in these patients remained elevated after surgery. Of 44 patients in complete remission, 20 showed a rise in marker levels an av 2.7 mo before clinical diagnosis of recurrence of NSTT. At 28 mo after treatment 84% of the 52 patients with Stage IIA disease were tumor-free. Of these patients 95% were with normalized marker levels, and 52% of the patients with abnormal marker levels were tumor free. Data indicate that measurement of AFP and b-HCG is a sensitive indicator for staging of NSTT, monitoring of the course of disease, and detection of recurrence. (10 Refs) (In GER)

37. EVALUATION OF PSBETA1G AND OTHER TUMOR MARKERS IN GERM CELL TUMORS OF THE TESTIS.

Blacker C, Feinstein MC, Roger M, Scholler R
(c/o Roger) 67 Bd. Pasteur, 94260 Fresnes, France
Andrologia; 13(5):458-467 1981

Radioimmunoassay was used to determine blood levels of pregnancy-specific beta1 glycoprotein, human chorionic gonadotropin, alpha-fetoprotein, and carcinoembryonic antigen in 58 patients with active testicular germ cell tumors and in 20 patients in complete clinical and radiological remission. The markers were negative in patients in remission and together showed a positive rate of 76% for patients with active germ cell tumors. (46 Refs)

38. THE ROLE OF ABDOMINAL SURGERY IN THE TREATMENT OF ADVANCED TESTICULAR GERM CELL TUMOURS.

Jones BM, Newlands ES, Begent RH, Rustin GJ, Johnson AG, Reynolds KW
Dept. Surgery, Charing Cross Hosp., Fulham Palace Road, London W6, England
Br J Surg; 69(1):4-6 1982

Twenty patients with advanced testicular teratoma and 1 with advanced seminoma have undergone abdominal surgery for the removal of residual disease following treatment by sequential chemotherapy. Fourteen out of the 21 patients (66%) have achieved complete remission with a follow-up period of 6-41 mo. In 12 patients (57%) the tumor had undergone histological maturation or necrosis following chemotherapy, those patients in whom the tumor remained histologically active having a worse prognosis. Raised preoperative serum levels of the tumor markers human chorionic gonadotrophin (hCG) and alpha-fetoprotein (AFP) indicating active disease, forecast a particularly poor prognosis, five out of nine such patients (55%) having died. Computerized tomography gave false negative results in three patients (14%). Postoperative complications were few, and only two patients (9%) suffered with failure of ejaculation. At present our policy is surgical removal of any residual mass after chemotherapy to determine the histology, and, wherever possible, to achieve complete clinical and biochemical remission. Six patients with an apparently poor prognosis have benefited directly from surgery and remain in long term remission. The selection of patients who benefit most from surgery can only be determined by more experience and longer follow up. (Author abstract) (19 Refs)

39. RADIATION THERAPY OF TESTICULAR NON-SEMINOMAS.

van der Werf-Messing B, Hop WC
Rotterdamsch Radio-Therapeutisch Instituut, Groene Hilledijk 301, 3075 EA Rotterdam, The Netherlands
Int J Radiat Oncol Biol Phys; 8(2):175-178 1982

Value of the primary radiotherapeutic approach was assessed in 121 patients with non-seminomatous germ cell tumors (NST) in various stages. Subgroups that might benefit from an initially combined modality treatment were identified according to stage and histology. Staging included laboratory tests for chorionic gonadotrophins and alpha fetoprotein. Extent of the disease was classified according to the Tumor, node, and metastasis-classification. At diagnosis significantly more patients in the malignant teratoma undifferentiated (MTU)-group were in a more advanced stage than patients in the malignant teratoma intermediate (MTI)-group. A routine dose of 4,000 rad was given to the target area in a period of approx 4 wk, by 5 fractions/wk. Actuarial survival rates were lower for both groups with increasing lymph node involvement (LNI); for most LNI-categories, patients with MTI had a better prognosis. The risk of pulmonary relapse (PR) was considerably higher in the MTU-group. In case of positive lymphangiography (LAG) the risk of PR was higher than with negative LAG for both MTI- and MTU-group. The group with a low risk of PR was composed of patients with either testis involvement or involvement beyond tunica albuginea, and a negative LAG; PR was approx 9% for both MTI- and MTU-groups. All other groups according to site involvement had a risk of PR of approx 50%. The significant risk difference between the total MTI- and MTU-groups is the result of a higher proportion of favorable patients in the MTI-group. (4 Refs)

40. CLINICAL ASSESSMENT OF PATIENTS WITH HEAD AND NECK CANCERS USING HEMATOLOGICAL, SEROLOGICAL, AND IMMUNOLOGICAL PARAMETERS.

Okamoto M
Dept. Otorhinolaryngology, Kitasato Univ. Sch. Medicine, Kanagawa 228, Japan
Nippon Jibiinkoka Gakkai Kaiho; 84(11):1408-1423 1981

Hematological, serological, and immunological parameters were assessed in 121 patients (92 men, 29 women) who had squamous cell carcinoma of the head and neck region and who were treated with either surgery or radiotherapy. Sites of cancers included the upper jaw in 29 of the patients, larynx in 45, upper pharynx in 18, middle pharynx in 5, cheek in 4, and others in 20. Peripheral blood lymphocyte count, T-cell count, and phytohemagglutinin blast-formation rate were used as parameters of cellular immunity. Serum immunoglobulins, complement components C3 and C4, CH50, carcinoembryonic antigen, and alpha-1-antitrypsin were used as parameters of humoral factors. Prior to treatment, the patients with pharyngeal cancer, advanced cancer, or poor prognosis frequently showed subnormal cellular immunity. Decreases in markers of cellular immunity varied according to treatment; marked decreases following treatment were observed particularly in patients with pharyngeal, upper jaw, or advanced cancer. The decreased cellular immunity following treatment improved rapidly after surgery but more slowly after radiotherapy. Hematological, serological, and immunological parameters must be considered along with appearance and functional preservation when treatment is being chosen for patients with head and neck cancers. (42 Refs) (In JPN)

41. BILATERAL JUVENILE GRANULOSA CELL TUMORS IN A 4-MONTH-OLD DYSMORPHIC INFANT: A CLINICAL, HISTOLOGIC, AND ULTRASTRUCTURAL STUDY.

Pyshcr TJ, Hitch DC, Krous HF
Dept. Pathology, Oklahoma Children's Memorial Hosp., P.O. Box 26307, Oklahoma City, OK, 73126
Am J Surg Pathol; 5(8):789-794 1981

A 4-mo-old girl with multiple congenital malformations presented with an abdominal mass. No history of prenatal drug or hormone exposure or abnormal postnatal endocrine activity existed. Serum alpha-fetoprotein (AFP) levels were mildly elevated (41.2 mg/ml). Sonography disclosed bilateral cystic ovarian masses and no signs of metastases. The ovarian masses were excised completely and identified as granulosa cell tumors. The patient had no evidence of disease and normal serum AFP level 16 mo postoperatively. Two other cases of bilateral juvenile granulosa cell tumors (both in young infants) have been reported. (21 Refs)

42. CARCINOEMBRYONIC ANTIGEN AND BETA2 MICROGLOBULIN IN MALIGNANT BONE DISEASES. 61 CASES.

Treves R, Clement A, Desproges-Gotteron R, Olivier JP, Beck C
Clinique Therapeutique et Rhumatologique, C.H.U. Dupuytren, rue Alexis Carrel, F 87000 Limoges, France
Nouv Presse Med; 11(1):21-24 1982

Radioimmunological assays of carcino-embryonic antigen (CEA) and beta2 microglobulin were carried out in 61 cases of malignant bone disease, including myeloma and metastases from carcinomas of the breast and prostate. CEA assays seemed to be of greater interest in mammary cancer metastases and beta2 microglobulin assays in prostatic cancer metastases and myeloma. The correlation which appeared between CEA levels and the outcome of breast cancer metastases was of assistance in adjusting treatment. Combining CEA and beta2 microglobulin assays would enhance their usefulness in current practice. (Author abstract) (17 Refs) (In FRE)

43. TWO PATIENTS WITH PANCOAST'S TUMOR SHOWING UNUSUAL SYMPATHETIC NERVE INVOLVEMENT.

Takezawa Y, Sakaguchi Y, Adachi E, Katada H, Sawaki M, Mikami R
Second Dept. Internal Medicine, Nara Medical Univ., Nara, Japan
Nara Igaku Zasshi; 32(5):461-466 1981

Two patients with Pancoast's tumor that had involvement of cervical and thoracic sympathetic nerves were reported. One patient, a 43-yr-old man with a history of renal calculi at age

28 and lung abscess at age 32, had primary complaints of warmth in the right upper arm, burning pain in the right upper arm when drinking alcohol, and pain radiating from the right shoulder girdle to the right upper arm. Clinical findings included lack of palpable lymph nodes and dry skin on the right side of the face, the right upper arm, and the right side of the chest above the fourth thoracic (T4) vertebra. The patient's right hand did not show perspiration. Roentgenography (plain and computed tomography) showed shadows in the T1-3 paravertebral region of the right chest. Exploratory surgery revealed an adenocarcinoma invading the periosteum. The patient was treated with radiotherapy and chemotherapy and died 4 yr 5 mo after diagnosis. The other patient, a 63-yr-old man, had primary complaints of right shoulder pain and burning sensation in the superior portion of the right chest. Clinical findings included increased skin temperature in the superior portion of the right chest, Gerstmann's syndrome, increased carcinoembryonic antigen levels, and tumor shadows in the apex of the right lung and left side of the brain. Aspiration biopsy of the chest tumor revealed a poorly-differentiated squamous cell carcinoma. The brain tumor was extirpated and was thought to be a metastatic nest of the lung carcinoma. The patient was treated with radiotherapy and chemotherapy but died 10 mo after diagnosis. Horner's syndrome was observed in the first patient but not in the second. (10 Refs) (In JPN)

44. CLEAR CELL ACANTHOMA: NOT OF SWEAT GLAND ORIGIN.

Penneys NS, Nadji M, Ziegels-Weissman J
Dept. Dermatology, Univ. Miami Sch. Medicine, Miami, FL, 33101
Acta Derm Venereol (Stockh); 61(6):569-570 1981

We have previously reported the presence of carcinoembryonic antigen in eccrine and apocrine gland and duct and in all sweat gland adenomas. The absence of carcinoembryonic antigen in clear cell acanthoma suggests that this lesion is not derived from sweat gland epithelium. (Author abstract) (6 Refs)

45. ECTOPIC HORMONE FORMATION IN MULTIPLE ENDOCRINE TYPE IIA NEOPLASIA.

Weber T, Cordes U, Eberle S, Rothmund M, Krause U, Beyer J
Abteilung fur Innere Medizin, Endokrinologie und Stoffwechsel, Universitat Mainz, Langenbeckstr. 1, 6500 Mainz 1, W. Germany
Dtsch Med Wochenschr; 107(7):252-256 1982

A patient with high-grade osteoporosis had elevated levels of ACTH, cortisol and carcinoembryonic antigen (CEA). Computed tomography demonstrated enlarged adrenal glands. Despite intensive search no ACTH-producing tumor was found. A central Cushing's syndrome was thus possible, and a radiologically normal sella turcica made a microadenoma of the hypophysis a possibility. However, a one-time hypertensive crisis with elevated catecholamines raised the suspicion of an additional pheochromocytoma and thus provided the first pointer to a multiple endocrine neoplasia. Bilateral pheochromocytomas, discovered at adrenalectomy, as well as raised serum-calcitonin levels, strongly suggested coexistence of a C-cell carcinoma, which previously had not been demonstrated either by thyroid scanning or fine-needle biopsy. A total thyroidectomy revealed a multifocal and metastasizing C-cell carcinoma. On extraction it contained a high concentration of calcitonin, typical for a C-cell carcinoma. An unusual finding was of ACTH in extracts of both the C-cell carcinoma and the pheochromocytoma. It was immunologically identical with the the synthetic ACTH used as a standard. (Author abstract) (30 Refs) (In GER)

ULTRASTRUCTURE/ CYTOCHEMISTRY

46. ATAXIA-TELANGIECTASIA: IMMUNOCYTOCHEMICAL DEMONSTRATION OF ALPHA-FETOPROTEIN AND HEPATITIS B SURFACE ANTIGEN IN THE LIVER.

Ohama E, Ikuta F
Dept. Neuropathology, Brain Res. Inst., Niigata Univ., Asahimachi 1, Niigata Cit y, 951, Japan
Acta Neuropathol (Berl); 56(1):13-16 1982

The liver, thymus and associated tumor tissue (adenocarcinoma of the stomach in 3 patients and medulloblastoma of the cerebellum in 1 patient) from five autopsy patients with ataxia-telangiectasia (AT) was examined for alpha-fetoprotein (AFP) and hepatitis B surface antigen (HBsAg) using the peroxidase-antiperoxidase method. AFP and HBsAg was detected in the cytoplasm of hepatocytes from all five patients but was not detected in the thymus or tumor tissue. The presence of AFP is consistent with the suggestion that AT patients have an underdevelopment of the liver. More striking is the detection of HBsAg in the absence of clinical or histological evidence of acute hepatitis B virus (HBV) infection in these patients. It is possible that persistent infection with HBV may play a role in the etiology and pathogenesis of AT. AT may be unique among immunodeficiency diseases and HBV carriers in its association with both AFP and HBsAg in the liver. (17 Refs)

47. IMMUNOCYTOCHEMICAL DETECTION OF TUMOUR MARKERS IN BONE METASTASES FROM CARCINOMA OF THE BREAST.

Gugliotta P, Botta G, Bussolati G
Istituto di Anatomia e Istologia Patologica, Univ. Turin, Turin, Italy
Histochem J; 13(6):953-959 1981

Immunocytochemical methods were employed for the detection of seven tumor-associated antigens in 10 cases of bone metastases from carcinoma of the breast. The biopsy specimens were fixed and decalcified in Bouin's soln using an apparatus which utilized ion-exchange resins. The following antisera were employed: anti-milk fat globule membrane (MFGM), anti-carcinoembryonic antigen (CEA), anti-human beta-casein, anti-human alpha-lactalbumin, anti-human chorionic gonadotropin (alpha subunit), anti-pregnancy-specific beta-1-glycoprotein, and anti-human placental lactogen. Application of immunoperoxidase methods to bone marrow was only possible after inhibition of endogenous peroxidase activity with periodic acid. With anti-MFGM serum metastatic neoplastic cells were detectable in all cases; the percentage of positive cells varied from case to case. CEA was detected in 9/10 cases. Casein was detected in only five cases; all other antisera were essentially negative. Most of the 10 cases of primary breast cancer were positive for MFGM, CEA, and casein; all were negative for lactalbumin and only one or two showed some neoplastic cells positive for at least one of the placental antigens. Therefore, MFGM and CEA appear to be the most useful markers for the identification of metastatic neoplastic cells in bone marrow originating from cancers of the breast. (23 Refs)

48. ULTRASTRUCTURAL LOCALIZATION OF ALPHA-FETOPROTEIN SYNTHESIS IN REGENERATING LIVER.

Baranov VN, Engel'gardt NV, Lazareva MN, Gusev AI
Lab. Cell Pathology and Electron Microscopy, Inst. Human Morphology, Moscow, USS R
Biull Eksp Biol Med; 91(12):736-738 1981

The electron microscope immunoperoxidase technic was used for the localization of alpha-fetoprotein (AFP) synthesis in regenerating liver of SWR mice. Liver regeneration was induced by exposure to carbon tetrachloride vapors. AFP was detected in very few hepatocytes adjacent to the zone of necrosis. AFP was present in the perinuclear space, and on the membranes and ribosomes of Golgi apparatus. (15 Refs) (In RUS)

REVIEWS/ OTHER RELATED STUDIES

49. THE ASSAY AND STRUCTURE OF CARCINOEMBRYONIC ANTIGENS.

Shively JE, Tood CW
City of Hope Res. Inst., Duarte, CA, 91016
The Handbook of Cancer Immunology: Volume 8- Tumor Antigens: Structure and Function. Waters H, ed. New York, STPM Garland Press, 418 pp., 1981.

The carcinoembryonic antigen (CEA) marker for colonic adenocarcinoma is occasionally found in other malignant and nonmalignant diseases. A similar but not identical substance has been obtained from normal colonic washings. CEA cross-reacting antigens have been obtained from liver metastases of colonic cancer; normal spleen, lung, granulocytes, and granulocyte-infiltrated tumor tissues; and hepatic bile. These antigens have nearly identical NH2-terminal sequences and similar polypeptide chains. They differ in the degree of glycosylation (which might be tissue-specific), contents of branched N-acetylglucosamine, certain amino acid substitutions, and tissue distribution. These antigens can be specifically measured in the nanog/ml range by sensitive immunoassays. The enzyme-linked immunoabsorbent assay methods may be a useful alternative to the competitive radioimmunoassay. Available evidence indicates that high-affinity anti-CEA antibodies recognize protein antigenic determinants in CEA, not carbohydrate determinants. A procedure that removes all carbohydrate except for asparagine-linked N-acetylglucosamine yields a CEA fraction which retains greater than 60% (by wt) of its original antigenic activity. Cleavage of CEA at its cysteinyl peptide bonds yields antigenically active peptides, which are difficult to sequence because their NH2-terminal residues are blocked. Tryptic digests of CEA have no antigenic activity. A synthetic NH2-terminal CEA peptide has some antigenic activity. (93 Refs)

50. DIFFERENTIAL EFFECTS OF SODIUM BUTYRATE, DIMETHYL SULFOXIDE, AND RETINOIC ACID ON MEMBRANE-ASSOCIATED ANTIGEN, ENZYMES, AND GLYCOPROTEINS OF HUMAN RECTAL ADENOCARCINOMA CELLS.

Tsao D, Morita A, Bella A, Luu P, Kim YS
(c/o Kim) Gastrointestinal Res. Unit, Veterans Admin. Medical Center, 4150 Clement St., San Francisco, CA, 94121
Cancer Res; 42(3):1052-1058 1982

The effects of sodium butyrate, dimethyl sulfoxide (DMSO), and retinoic acid on the growth, morphology, carcinoembryonic antigen content, cell surface membrane-associated enzyme activities, and glycoprotein profiles of a human rectal adenocarcinoma cell line (HRT-18) in culture were compared. All three agents reversibly caused a marked increase in doubling times, a decrease in saturation densities, and a markedly reduced colony-forming efficiency in soft agar. Only butyrate caused gross morphological changes including cell enlargement, flattening, and increased membranous process formation. Carcinoembryonic antigen content was increased during culture in butyrate, while it was reduced by DMSO and unchanged by retinoic acid. The activities of membrane-associated enzymes were altered significantly in the butyrate-treated cells. For example, an increase in the activities of alkaline phosphatase (10-fold), gamma-glutamyl transpeptidase activity (3-fold) and sucrase activity (2-fold) was observed, while those of aminooligopeptidase and K+-stimulated phosphatase actually showed slight decreases. DMSO- or retinoic acid-treated cells showed a marked decrease in alkaline phosphatase activity, but other enzyme activities remained unchanged. Surface protein-labeling patterns of lactoperoxidase-catalyzed iodinated HRT-18 cells showed no significant change from the control cells following treatment with DMSO or retinoic acid. The most prominent change caused by butyrate treatment was the appearance of a major glycoprotein band with an apparent mol wt of 60,000. These data indicate that the use of butyrate, DMSO, and retinoic acid may provide useful information concerning the identification of differentiation-associated markers of human rectal cancer cells. Furthermore, these agents, although having similar effects on the growth properties, have different effects on the morphology and on the biochemical properties of human rectal cancer cells. (Author abstract) (48 Refs)

51. CHARACTERIZATION OF A NEWLY ESTABLISHED HUMAN GASTRIC CANCER CELL LINE HGT-1 BEARING HISTAMINE H2-RECEPTORS.

Laboisse CL, Augeron C, Couturier-Turpin MH, Gespach C, Cheret AM, Potet F

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Cancer Res; 42(4):1541-1548 1982

A human gastric adenocarcinoma cell line, HGT-1, was established in vitro from the primary tumor of a 60-yr-old patient. Histological examination of the tumor revealed a poorly differentiated adenocarcinoma. Primary tumor cells were cloned in soft agarose and gave rise to tumor colonies. The procedures enabling us to form a continuous cell line from the agarose colonies are described. The cultured cells grew as monolayers of closely apposed polygonal cells with a population-doubling time of 19.48 +-1.20 (SE) hr during exponential growth at passage 59. They had an epithelial morphology. Ultrastructural studies revealed the presence of microvilli and tight junctions. The HGT-1 cell line is tumorigenic in nude mice and has a hyperdiploid karyotype with a modal number of 57 chromosomes. It exhibits numerous marker chromosomes. These human gastric epithelial cells do not secrete mucus or carcinoembryonic antigen. They exhibit functional histamine H2-receptors mediating cellular cyclic adenosine 3':5'-monophosphate production and adenylate cyclase activation. In conclusion, the use of a soft-agarose clonogenic assay permitted us to develop a cancer cell line without the problems of fibroblastic cell contamination. The existence of histamine H2-receptors on gastric HGT-1 cells stresses the importance of this line as a model for studies of regulatory mechanisms involved in gastric secretion. (Author abstract) (39 Refs)

52. LACK OF ASSOCIATION OF CYTOMEGALOVIRUS WITH ADENOCARCINOMA OF THE COLON.

Hart H, Neill WA, Norval M
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Gut; 23(1):21-30 1982

Tumor specimens from patients with adenocarcinoma of the colon or rectum were examined for the presence of cytomegalovirus (CMV), and specimens of normal mucosa from the same patients were studied in parallel. Frozen sections of 14 specimens were made and the presence of CMV mRNA assayed by in situ hybridization using 3H-labeled CMV-DNA as a probe. Nine of these sections were also tested for cytomegalovirus antigens by immunofluorescence. No viral nucleic acids or antigens were detected. In addition to these direct approaches, the specimens were disaggregated and 19 were successfully cultured in various media over several months without yielding virus on any occasion. Areas containing epithelial cells were found in some cultures, foci of bipolar cells in others, while, in several, fibroblastic cells predominated. To ensure that any virus-containing cells were not lost by this method, the disaggregated tumor and normal intestinal cells were directly co-cultivated and also fused with human embryo lung cells, which are permissive for cytomegalovirus replication. The resulting cultures were examined over 2 to 3 mo for the presence of cytomegalovirus, and in no instance was virus found, despite attempted induction by iododeoxyuridine. Two fusion cultures became contaminated with cytomegalovirus, strain AD-169, which was being handled in the laboratory at the same time. The strain was identified by the pattern of viral DNA fragments produced by restriction endonuclease cleavage. Thus the accidental passage of virus in the heterokaryons did not alter its DNA and would further indicate the absence of any cytomegalovirus genomes in the adenocarcinoma cells. (Author abstract) (34 Refs)

53. TRENDS IN CANCER RESEARCH ON CANCER FETOPROTEINS AS MARKERS.

Nishi S, Hirai H
Dept. Biochemistry, Yamanashi Medical Coll., Kofu, Japan
Nippon Rinsho; 39(10):3323-3329 1981

Discussions concerning two or three topics related to alphafetoprotein (AFP) and carcinoembryonic antigen (CEA) chosen from cancer research studies on cancer fetoproteins used as markers, are presented. Potential for increasing the diagnostic value of serum AFP measurements was discussed. Research indicates that yolk sac tumor and hepatoma can be distinguished by analysis of serum AFP; differentiation of metastatic liver cancer and liver cancer is also thought to be possible with this method. Common bean lectin-ligated AFP, not found in benign hepatic disease, was thought to be very important for early detection of hepatic cancer and for research of precancerous conditions of hepatic cancer. The lectin-affinoelectrophoresis method was thought to be an effective method for detecting differences in lectin ligands of AFP. Clinical and experimental trials of tumor radioimmunodetection with anti-CEA antibody and anti-AFP antibodies indicated that in order to maximize results, the antibody that has the highest tumor-cell blocking activity or the highest accumulating activity around the tumor cells should be used. Then, the antibody with the highest affinity for the tumor cells should be used in selecting the most appropriate antineoplastic or cytotoxic chemotherapy for the patient. (24 Refs) (In JPN)

54. BIOLOGIC MARKERS IN LUNG CANCER.

Vincent RG
Dept. Thoracic Surgery and Oncology, Roswell Park Memorial Inst., 666 Elm St, Buffalo, NY, 14263
Semin Respir Med; 3(3):184-193 1982

Specific biologic markers in lung cancer may be more commonly related to one histologic type of lung cancer than another. Such markers are classified as hormones, antigens, enzymes or proteins. The presence of tumor markers might permit screening for early malignant lesions,monitoring of the clinical course of previously diagnosed and treated tumors, or establishment of a selective differential diagnosis. Hormonal tumor markers include calcitonin, ACTH, lipotropin, parathyroid hormone, antidiuretic hormone, growth hormone, human chorionic gonadotropin, placental lactogen, melanocyte-stimulating hormone, prolactin, and 5-hydroxytryptophan. Proteins, antigens and antibodies that have been identified as possible tumor markers include ceruloplasmin, ferritin, tissue polypeptide antigen, Tennessee antigen, alpha 1-antitrypsin, carcinoembryonic antigen, pancreatic oncofetal antigen, beta 2-microglobulin, immunoglobulins, and alpha fetoprotein. Enzymes that may be useful as tumor markers include 5'-nucleotide phosphodiesterase isozyme-V, galactosyl-transferase II, amylase, creatine kinase, sialyltransferase, and placental alkaline phosphatase. Some of the nonspecific markers individually or in combination may be useful in the future in diagnosis, staging and therapy of lung cancer. (136 Refs)

55. HUMAN COLON TUMOR ANTIGENS.

Yeoman LC, Taylor CW, Chakrabarty S
Nuclear Protein Lab., Dept. Pharmacology, Baylor Coll. Medicine, Houston, TX, 77030
Methods Cancer Res; 19:233-271 1982

Colon cancer marker biology, cellular fractionation and antibody preparation, radioimmunoelectrophoresis, immunolocalization of GW-39 hamster colon tumor antigens, and purification and properties of colon antigens are reviewed. Subcellular fractionation of GW-39 colon adenocarcinoma cells into cytoplasmic and nuclear fractions yielded extracted antigens, which may have been dominated by other molecules when presented to a xenogeneic host as a group. Three potential antigen markers have been detected which share no immunological cross-reactivity with carcinoembryonic antigen. One of these, antigen 3, a glycoprotein of approx 150,000 mol wt, is most highly purified and characterized to date. Cancer marker molecules aid in the investigation of the biological mechanism involved in tumor promotion, carcinogenesis, or maintenance of cancer phenotype. (91 Refs)

56. TUMOR ASSOCIATED IMMUNOSUPPRESSIVE SERUM PROTEINS.

Ninnemann JL
Dept. Surgery, Sch. Medicine, Univ. California, San Diego, CA, 92037
The Handbook of Cancer Immunology: Volume 8- Tumor Antigens: Structure and Function. Waters H, ed. New York, STPM Garland Press, 418 pp., 1981.

A tumor-associated immunosuppressive factor (ISF) or complex of factors was isolated from the sera of patients who had been treated only by surgery for advanced melanomas (Clark's Level IV-V) up to 2 yr previously. Serum ISF levels were significantly elevated in 7/14 patients; 3/7 later died, and 2/7 others showed marked increases in serum ISF activity as their tumors spread. The other 7/14 patients were all alive at the time of report. The immunosuppressive effects (in vitro) of preoperative sera were often inhibited by non-immunosuppressive autologous sera obtained 2-3 wk postoperatively. Anti-immunosuppressive antibodies were found in the non-immunosuppressive sera. Preliminary analytical studies identified this ISF as an immunogenic substance; probably a protein; probably of high mol wt; extremely stable to heat but inactivated by prolonged freezing or repeated freeze-thawing; unrelated to RNA, DNA, or cortisol; not an immunoglobulin (Ig); and not alpha-2-macroglobulin (A2MG) although possibly associated with A2MG. This ISF may be only one of many tumor-associated immunosuppressive factors recoverable from the sera of patients with advanced cancer (Ig, immune complexes, alpha-globulin, prostaglandins, carcinoembryonic antigen, and histamine are reportedly involved). However, there are several possible sources of misleading information in the search for immunosuppressive tumor-associated serum components, which are discussed. (120 Refs)

57. THE HANDBOOK OF CANCER IMMUNOLOGY: VOLUME 8: TUMOR ANTIGENS: STRUCTURE AND FUNCTION.

Waters H
NIH, Bethesda, MD
The Handbook of Cancer Immunology: Volume 8: Tumor Antigens: Structure and Function. New York, Garland STPM Press, 418 pp., 1981.

Structural and functional aspects of tumor antigens are reviewed. Mechanisms of reactions between lymphocytes and antigens are discussed. Characteristics of Ia antigens in mice and humans are presented and the significance of these antigens is considered. Histocompatibility antigens and tumor-associated antigens in plasma and urine are discussed and their diagnostic significance evaluated. Molecular structure and mechanisms of antibody-antigen interactions are outlined. Other topics include the use of cell membranes to assess phenotypic expression, masking of cancer-cell surface antigens, cell surface modulation in mammary cancer, antigen activation of T cells, assay and structure of carcinoembryonic antigens, induction of immune response to tumors induced by simian virus 40, and tumor-associated immunosuppressive serum proteins. Concentration and distribution of antigens are related to normal and pathological conditions. Discussion includes review of literature, presentation of original findings, and speculation on future research efforts. Converging and diverging viewpoints are expressed. (1659 Refs)

58. LONG-TERM EFFECTS OF AZATHIOPRINE IN RHEUMATOID ARTHRITIS.

Urowitz MB, Smythe HA, Able T, Norman CS, Travis C
Rheumatic Disease Unit, Wellesley Hosp., 160 Wellesley St. E., Toronto, Ontario, M4Y 1J3, Canada
Ann Rheum Dis; 41(Suppl1):18-22 1982

Potential early signs of malignancy were assessed in 36 patients (8 men, 28 women; mean age 57.8 yr) receiving azathioprine (APR: mean, 1.08 mg/kg/day x 38.5 mo) for rheumatoid arthritis and 49 controls (13 men, 36 women; mean age 51.4 yr) not receiving APR. The mean duration of arthritis was somewhat longer in the APR group (15.3 vs 11.9 yr). The groups were comparable in their symptomatic status, chest x-rays, and most laboratory test results. As compared to the controls, the APR groups showed significantly lower WBC counts, a higher frequency of megaloblastic features in the bone marrow, lower serum folate levels, and a higher frequency of chromosomal aberrations in the bone marrow. Malignancies had occurred in first-degree relatives of 15/36 APR-treated patients and 6/49 controls. The APR and control groups showed comparable frequencies of inflammatory or fibrotic pulmonary abnormalities (15/36 vs 9/49), benign breast masses (1/28 vs 3/36 women), and abnormal urine cytology (4/36 vs 1/49) with no evidence of cancer on follow-up. Neoplasms were observed in 7/36 APR patients (3/7 were malignant or potentially malignant tumors) and 5/49 controls (1/5 was a malignant tumor); the difference in incidence rates were not significant. The only non-Hodgkin's lymphoma observed in the group was in a control patient. In the APR group, the tumors developed after a mean of 1.6 yr of APR therapy. Three APR-treated patients with cancer had positive family histories of cancer; none of the controls with tumors had family histories of cancer. Elevated titers of alpha-fetoprotein or carcinoembryonic antigen were observed in some of the APR group (1/36 and 7/25 patients tested, respectively; none of these patients had a detectable cancer) and none of the controls. Further studies in larger groups of APR-treated patients and longer treatment periods are recommended. (53 Refs)

59. TUMORAL IMMUNOLOGY III. IMMUNOLOGY IN MAMMARY CANCER.

Crisci CD
Catedra de Neumonologia, Alergia e Inmunologia Clinica, Facultad de Ciencias Medicas, U.N.R., Rosario, Argentina
Rev Fac Cienc Med Univ Nac Rosario; 14(2):34-45 1981

Immunology in mammary cancer was reviewed under the following headings: antigen associated with tumors (AAT) in mammary cancer (MC), carcinoembryonic antigen (CEA), response to the AAT in MC (humoral and cellular responses; blocking factors), evaluation of the immune (IM) system in MC (subpopulations of lymphocytes, lymphoproliferative response to mitogens, delayed hypersensitivity in vivo, and immunoglobulins), and evaluation of IM state and of levels of CEA in MC in relation to tumoral spreading and evolution after surgery and radiotherapy (IM state at time of diagnosis, IM state immediately after the surgery, evolution of the IM state after treatment, and CEA). (242 Refs) (In SPA)

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STRUCTURE/ IDENTIFICATION/ CHARACTERIZATION

1. IMMUNOLOGICAL CHARACTERIZATION AND STRUCTURAL STUDIES OF NORMAL FECAL ANTIGEN-1 RELATED TO CARCINOEMBRYONIC ANTIGEN.

Kuroki M, Shinoda T, Takayasu T, Koga Y, Matsuoka Y
(c/o Matsuoka) First Dept. Biochemistry, Sch. Medicine, Fukuoka Univ., 34 Nanakuma, Nishi-ku, Fukuoka 814-01, Japan
Mol Immunol; 19(3):399-406 1982

Normal fecal antigen-1 (NFA-1), which is a carcinoembryonic antigen (CEA)-related glycoprotein with a mol wt of 20,000-30,000 was purified from normal adult feces by immunoadsorption, gel filtration and ion exchange chromatography. Highly purified NFA-1 was partially cross-reactive with CEA but antigenically unrelated to nonspecific cross-reacting antigen (NCA) which was also cross-reactive with CEA. NFA-1

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also had a unique determinant not present in CEA or other related antigens including NCA. In a solid-phase RIA system, the reactivity of NFA-1 with a specific anti-CEA antiserum was much stronger than that of NCA. Although digestion with Pronase E did not affect the antigenicity of NFA-1, reduction and alkylation destroyed its antigenic reactivity. The total amount of carbohydrate in NFA-1 was 13.3% compared to 52.4% in CEA and 21.6% in NCA. The amino acid composition of NFA-1 was similar to that of CEA. The sequence of the first 10 NH2-terminal amino acids in NFA-1 was Ala-Glu-Pro-Pro-Lys-Pro-Phe-Ile-(Thr)-Ser. This was totally different from that of the first NH2-terminal amino acids of CEA isolated from tumor tissue. (Author abstract) (30 Refs)

2. RADIOIMMUNOLOGICAL CHARACTERIZATION OF CARCINOEMBRYONIC ANTIGEN (CEA) PREPARATIONS.

Zotter S, Heidl G, Grossmann H, Muller M, Johannsen BA, Pilz C
Inst. Pathology, Medical Acad. Carl Gustav Carus, Fetscherstrasse 74, DDR-8019 Dresden, E. Germany
Exp Pathol; 21(1):10-20 1982

A multi-step radioimmunological test system was applied to the characterization of carcinoembryonic antigen (CEA) preparations obtained by column chromatography including ion exchange procedure. CEA contents were estimated by means of a sequential inhibition radioimmunoassay using Protein A-bearing Staphylococci for coprecipitation. Data were expressed as 'units CEA' and compared with results obtained from commercial CEA-RIA kits. In addition, attempts were made to evaluate the presence of normal cross-reacting antigens in CEA preparations by the application of an antiserum to perchloric acid extract from normal lung tissue. Data from these tests were expressed as 'units NLA' (NLA stands for 'normal cross-reacting lung antigen'). The factor 'units CEA/units NLA' proved useful as an indication of the tumor specificity of those antigenic components measured in the inhibition assay. Moreover, radioimmunoprecipitation tests with subsequent SDS polyacrylamide gel electrophoretic analysis were performed in order to get information on the mol wt of the molecule(s) involved in the radioimmunological CEA determination procedure. The test system displayed (1) highly specific CEA reagibility in the standard inhibition assay, (2) test sensitivity of about 200 pg CEA (when related to the Hoffman/La Roche test) and 1 ng CEA (when related to CEA-IRE-SORIN), (3) low reagibility to normal cross-reacting antigens, also when compared to the commercial tests, (4) a mol wt of about 200,000 daltons for the component(s) measured, and (5) evidence of inhomogeneity of the CEA batches investigated and those international references available. The latter might in part be attributed to so-called species-specific CEA-related determinants. The test system proved also useful for CEA estimations in crude tissue extracts. (Author abstract) (26 Refs)

3. CARBOHYDRATE STRUCTURE OF THE CONCANAVALIN A MOLECULAR VARIANTS OF ALPHA-FETOPROTEIN.

Krusius T, Ruoslahti E
Dept. Medical Chemistry, Univ. Helsinki, Siltavuorenpenger 10, SF 00170 Helsinki 17, Finland
J Biol Chem; 257(7):3453-3457 1982

The structure of the carbohydrate units of alpha-fetoprotein from fetal calf serum has been studied. Glycopeptides and oligosaccharides were prepared from alpha-fetoprotein by protease treatment and hydrazinolysis, respectively, and subjected to carbohydrate and amino acid analysis. Two N-glycosidic glycans are present in each alpha-fetoprotein molecule. These were separated into concanavalin A (ConA)-reactive and nonreactive species on ConA-Sepharose. Methylation analysis, Smith degradation, sequential exoglycosidase treatments, and sizing suggested that the major, ConA-nonreactive fraction is composed of triantennary and the minor, ConA-reactive fraction, of biantennary complex-type glycans. Oligosaccharides were prepared from the ConA-reactive and -nonreactive fractions of intact alpha-fetoprotein, respectively, and refractionated on Con A-Sepharose. The results indicate that 75% of alpha-fetoprotein molecules contain two triantennary complex-type glycans, 20% contain one triantennary and one biantennary glycan, and 5% contain two biantennary glycans. The last two molecular variants are bound to ConA. These results explain, at least in part, the previously found heterogeneity of alpha-fetoprotein with respect to charge and molecular size, and provide a biochemical basis for the differing reactivities toward ConA of alpha-fetoprotein from the yolk sac, fetal liver, and various tumors. (Author abstract) (51 Refs)

4. MONOCLONAL ANTIBODIES AGAINST CARCINOEMBRYONIC ANTIGEN.

Hedin A, Hammarstrom S
Dept. Immunology, Univ. Stockholm, Stockholm, Sweden
Protides Biol Fluid Proc Colloq; 29:907-910 1982

Monoclonal antibodies against carcinoembryonic antigen (CEA) were produced using a hybridoma technique. Spleen cells from BALB/c mice immunized with highly purified CEA were fused with mouse myeloma cell line Sp2/0-Ag 14. Data on eight monoclonal antibodies against CEA obtained from cells cultured for 4 mo are reported. All eight antibodies were IgG 1 and six showed different isoelectric points. Three different titration curves of supernatant reactivity were seen. Six of the eight antibodies were directed against conformation dependent epitopes on the CEA molecule since they showed a marked decrease in reactivity against reduced and alkylated CEA as compared to the native molecule. All antibodies showed approx equal reactivity against Smith degraded CEA compared to native CEA. It was concluded that the antibodies were directed against the protein moiety of the molecule. One antibody gave a precipitate when tested in immunodiffusion against CEA; however, when two different antibodies were combined and tested against CEA, strong precipitates were seen in several combinations. Thus, at least five antibodies recognize different epitopes on the CEA molecule. (6 Refs)

ASSAY PROCEDURES/ SYNTHESIS

5. A SEMI-AUTOMATED ENZYME-LINKED IMMUNOSORBENT ASSAY (ELISA) TO SCREEN FOR HYBRIDOMA CULTURES PRODUCING ANTIBODY TO CARCINOEMBRYONIC ANTIGEN.

Woodhouse CS, Ford CH, Newman CE
Surgical Immunology Unit, Clinical Oncology, Univ. Birmingham, Queen Elizabeth Hosp., Birmingham, England
Protides Biol Fluid Proc Colloq; 29:641-644 1982

An enzyme-linked immunosorbent assay method for detection of mouse antibody to carcinoembryonic antigen (CEA) is described which is capable of detecting 50 picog/cuvette of monoclonal antibody to CEA. Culture supernatants or samples were incubated in CEA-coated cuvettes. Antibody attached to

HE 20.3173/2:

this solid phase was subsequently detected with the use of anti-mouse immunoglobulins conjugated to horseradish peroxidase. The use of automated washing and absorbance determination provided greater standardization and simplified the screening of large numbers of cultures. (5 Refs)

6. CHARACTERISATION OF MONOCLONAL ANTIBODIES TO CARCINOEMBRYONIC ANTIGEN BY ANTIBODY OVERLAY OF POLYACRYLAMIDE SLAB GELS.

Chester KA, Begent RH

Dept. Medical Oncology, Charing Cross Hosp., London W6 8RF, England

Protides Biol Fluid Proc Colloq; 29:911-914 1982

Two monoclonal antibodies (MS1 and MS200) taken from BALB/c mice bearing myeloma cells in ascites form were produced against carcinoembryonic antigen (CEA) and their binding characteristics studied. CEA samples from different sources were subjected to sodium dodecyl sulfate polyacrylamide slab gel electrophoresis (SDS PAGE) and the separated tracks were overlaid with serum from MS1, MS200 or normal mice. Binding of the monoclonal antibodies to components of different mol wt was demonstrated by autoradiography after overlay with 125I-labeled antibody directed against mouse IgG. Different binding patterns were observed with different antibodies in the same CEA preparation and with the same antibody in different CEA preparations. The epitope with which MS200 reacted seemed to be expressed more often on the lower mol wt component than the higher component, while that reacting with MS1 was equally represented on both peaks. Thus, MS1 and MS200 have different binding characteristics to the same CEA preparation, and the two antibodies are specific for different epitopes. The value of this technique for characterization of monoclonal antibodies and protein antigens is evident. (4 Refs)

EXPERIMENTS IN ANIMAL SYSTEMS

7. EVIDENCE FOR A NOVEL CIRCULATING ALPHA1 PROTEIN IN TUMOR-BEARING RATS. DIFFERENTIATION FROM ACUTE PHASE ALPHA1 PROTEINS AND FROM ALPHA1 FETOPROTEIN.

Herve F, Urios P, Grigorova AM, Cittanova N, Rondeau Y, Engler R, Broadhead G, Neish W

Equipe de Recherche No. 239, Centre National de la Recherche Scientifique, Universite Paris V., Paris, France

Biochem Biophys Res Commun; 105(3):861-868 1982

The isolation of a novel alpha1 protein (AP) from an experimental RD/3 rat sarcoma is described, and evidence that it is molecularly distinct from both acute phase AP and alphafetoprotein is presented. This new protein component may be linked to the development of the RD/3 tumor and may correspond to a tumoral protein. The presence of this protein may play a role in the modification of the transport properties of animals bearing an RD/3 tumor. (14 Refs)

8. ALPHA-FETOPROTEIN SYNTHESIS IN PRIMARY CULTURES OF HEPATOCYTES OF ADULT MICE.

Gleiberman AS

Lab. Immunochemistry and Tumor Diagnosis, All-Union Cancer Res. Center, Moscow, USSR

Biull Eksp Biol Med; 92(1):55-58 1982

To determine whether the biosynthesis of alpha-fetoprotein (AFP) is associated with local disturbances of interhepatocyte contacts, AFP and albumin synthesis were studied in primary cultures of hepatocytes of adult C57Bl/6J, SWR, BALB/c, and (C57BL/6J x CBA)F1 mice. Immunoperoxidase staining showed the presence of AFP-containing hepatocytes starting from day 3 of culturing. Significant numbers of AFP-containing hepatocytes were observed on day 5. AFP synthesis in the cultured C57BL/6J hepatocytes was similar to that in the cultured SWR hepatocytes, while in vivo AFP synthesis in regenerating liver of the C57BL/6J mice was 10x lower than that in the regenerating liver of the SWR mice. (14 Refs) (In RUS)

9. NO EVIDENCE FOR POST-TRANSCRIPTIONAL CONTROL OF ALBUMIN AND ALPHA-FETOPROTEIN GENE EXPRESSION IN DEVELOPING RAT LIVER AND NEOPLASIA.

Nahon JL, Gal A, Frain M, Sell S, Sala-Trepat JM

Laboratoire d'Enzymologie, CNRS, 91190 Gif-sur-Yvette, France

Nucleic Acids Res; 10(6):1895-1911 1982

Rot analysis of hybridization data using highly labeled alpha-fetoprotein (AFP) and albumin (32P)cDNA probes has been used to quantitate AFP and albumin mRNA sequences in RNA preparations from different subcellular fractions of developing rat liver and Morris hepatoma 7777. In addition, size analysis of these mRNA sequences has been carried out by electrophoretic fractionation on agarose gels containing methylmercury hydroxide and hybridization to radioactive cloned albumin and AFP cDNA probes. In all the tissues examined (fetal, newborn and adult rat liver, and hepatoma 7777) most of the albumin and AFP mRNA sequences were found associated with the polysomes as mature mRNA molecules; less than 2% of these sequences were present in the nuclear or the nonpolysomal cytoplasmic compartments. The number of AFP mRNA molecules was found to decrease in parallel in all the cellular compartments during rat liver development. In Morris hepatoma 7777 the content of albumin mRNA was considerably decreased in all the cellular fractions as compared to normal liver. These results demonstrate that post-transcriptional control mechanisms leading to an accumulation of non-functional mRNA molecules are not implicated in the changes of expression of albumin and AFP genes during rat liver development and neoplasia. (Author abstract) (47 Refs)

10. HUMAN GYNECOLOGIC CANCERS HETEROTRANSPLANTED INTO ATHYMIC NUDE RATS.

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Gynecol Oncol; 13(2):220-228 1982

The serial transplants of human ovarian and endometrial tumors in nude mice were transplanted into nude rats. The transplants consisted of three lines of yolk sac tumors, designated a YST-1, YST-2, and YST-3. and two lines of endometrial adenocarcinoma, AD-30 and AD-35. The transplanted tumors grew much larger in nude rats than in nude mice, reaching more than 150 g in wt. The overall grafting success rate of these tumors was about 70% in nude rats whereas it had been almost 100% in nude mice. The histology of the transplanted tumor in nude rats was similar to that of the same tumor in nude mice. YST-1, YST-2, and YST-3 tumors produced the marker alpha-fetoprotein (AFP). Thus the transplanted tumors in nude rats seemed to preserve the characteristics of the original tumors. The usefulness of the nude rat as a tool for studying the efficacy of treatments on human malignant tumors is discussed. (Author abstract) (9 Refs)

11. INFLUENCE OF METHIONINE ADMINISTRATION ON SERUM ALPHA-FETOPROTEIN LEVELS IN ETHIONINE-INJURED RATS.

Miyazaki M, Watanabe A, Wahid S, Tsunashima M, Sato J
Div. Pathology, Cancer Inst., Okayama 700, Japan
Res Exp Med (Berl); 180(1):15-19 1982

A single injection of ethionine (100 mg/100 g body wt) caused serum alpha-fetoprotein (AFP) levels to sharply increase in female adult Sprague rats 2 days later, reaching a max at 4 days, and then decreasing. After ingesting a diet containing 1% ethionine for 3 wk serum AFP constantly increased to a max level of 800 nanog/ml. Supplementing the ethionine diet with 2.8% methionine resulted in slightly elevated AFP on day 4, but no further elevation. (17 Refs)

12. EFFECT OF CYCLOPHOSPHAMIDE ON THE ALPHA-FETOPROTEIN LEVEL IN BLOOD SERA OF MICE BEARING HEPATOMA 22A AT DIFFERENT STAGES OF TUMOR DEVELOPMENT.

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Dept. Biology, N. I. Pirogov Second Medical Inst., Moscow, USSR
Biull Eksp Biol Med; 92(1):60-62 1982

The relationship between efficacies of antineoplastic agents and periods of tumor development was studied in male C3HA mice bearing hepatoma 22A. Within different time periods after tumor transplantation, the animals were injected with cyclophosphamide (CP, 100-150 mg/kg, sc). The blood level of alpha-fetoprotein (AFP) was determined by double immunodiffusion assay. In nontreated mice, the AFP was first detected on day 8 after tumor transplantation. Level of the AFP showed a progressive increase and reached a max on day 14. A second increase in AFP level was observed on day 19. CP administration on day 6 of tumor development caused a 4x decrease in AFP level. CP administration on day 7 did not affect the AFP level, while CP administration on days 11 or 16 caused an increase in the level. The most pronounced inhibition of AFP level was observed after CP administration on day 4. (6 Refs) (In RUS)

IMMUNOLOGIC INTERACTIONS

13. SENSITIZATION OF HUMAN LYMPHOCYTES TO CARCINOEMBRYONIC ANTIGEN (CEA): NEUTRALIZATION EXPERIMENTS WITH ANTI-CEA SERA.

Muller M, Irmscher J, Heidl G, Grossmann H, Wagner H, Kotzsch M, Zotter S
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Exp Pathol; 21(1):5-9 1982

By means of the macrophage electrophoretic mobility technique we could show lymphocytes of patients suffering from cancers of the digestive system to be sensitized to carcinoembryonic antigen (CEA). These findings conflict with the common view that CEA is not immunogenic in humans. The aim of the present study was to look as to whether conventional anti-CEA sera can neutralize the activity of a CEA preparation which is responsible for the human lymphocyte response. When 60 ng CEA were preincubated with highly diluted anti-CEA serum and the resulting immune complexes were thereafter co-precipitated by protein A-sepharose, positive lymphocyte responses could no longer be obtained. This effect was observed with three anti-CEA sera in three cancer patients (colon cancer, stomach cancer, teratocarcinoma), who's lymphocytes responded to CEA by lymphokine release. Normal serum had no neutralizing effect. The anti-CEA sera did not influence the activity of another tumor-relevant extract (teratocarcinoma-derived), to which cancer patients' lymphocytes reacted regardless of the tumor site. The lymphocytes from an esophagus carcinoma patient, though reacting to the teratocarcinoma preparation, did not respond to CEA, thus, logically, all other tests with normal serum and anti-CEA sera were negative, too. The results show that the digestive system cancer-associated lymphocyte reactivity to CEA can be abrogated by conventional anti-CEA sera, which finding indicates that there exist closely CEA-associated 'tumor-specific' antigenicities. (Author abstract) (18 Refs)

14. COMPARISON OF EFFECTS OF LEUKOCYTE AND FIBROBLAST INTERFERON ON IMMUNOLOGICAL PARAMETERS IN CANCER PATIENTS.

Lucero MA, Magdelenat H, Fridman WF, Pouillart P, Billardon C, Billiau A, Cantell K, Falcoff E
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Eur J Cancer Clin Oncol; 18(3):243-251 1982

Patients with metastastic cancer were given single intramuscular injections of 10(7) units of partially purified preparations of either leukocyte or fibroblast IFN. Serum levels of interferon, of beta2-microglobulin and of carcino-embryonic antigen (CEA), as well as NK activity of circulating lymphocytes, were followed over a period of 96 hr post injection. In confirmation of previous studies, levels of circulating IFN were lower after injection of fibroblast IFN than after injection of leukocyte IFN. Despite this difference in pharmacokinetics, the natural killer activity of circulating lymphocytes was enhanced with both IFNs. Levels of CEA were not influenced by the IFN injections. Leukocyte but not fibroblast IFN caused an increase in serum levels of beta2-microglobulin in the circulation. A similar difference between leukocyte and fibroblast IFN in their ability to influence the beta2-microglobulin system was observed in experiments on cell cultures. Only leukocyte IFN was able to cause release of beta2-microglobulin by either leukocytes or fibroblasts. (Author abstract) (32 Refs)

15. COMPARISON OF THE TECHNIQUES USED FOR MONITORING HUMORAL IMMUNITY IN CANCER PATIENTS.

Renk CM, Gupta RK, Irie RF, Morton DL
Dept. Surgery, Medical Coll. Ohio, Toledo, OH, 43699
J Surg Oncol; 19(3):155-161 1982

The humoral immune response to tumor-associated antigens (TAA) in cancer patients undergoing immunotherapy can vary considerably. This variability is inherent from patient to patient and is also dependent on the type of assay used to measure patient antibody response to tumors. In this investigation four serological techniques, complement-dependent antibody-mediated cytotoxicity, immune adherence, complement fixation, and indirect membrane immunofluorescence, were used to assess the humoral immune response in melanoma patients receiving specific immunization with cultured allogeneic melanoma cell vaccine. Two different patterns of antibody response were elicited. One was directed against TAA and oncofetal antigens (OFA) and the other was against HLA antigens. The sensitivity and reactivity varied among the different techniques suggesting that one test or technique may not be sufficient to evaluate critically a patient's response to immunotherapy. (Author abstract) (18 Refs)

CLINICAL/ DIAGNOSIS/ IMMUNOTHERAPY

16. CEA SERUM VALUES CONTROVERSY.

Satler JJ, Herzog B
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Am J Proctol Gastroenterol Colon Rectal Surg; 33(2):24,26,28 1982

Considering the hypothesis that the CEA concentrations in serum might be in proportion with CEA concentrations in malignant tissue of patients with proven colorectal carcinoma, thus explaining different normal as well as pathological values in sera, 23 radically operated patients were selected for the study. Both concentrations were estimated using radioimmunoassay of double antibodies and the values of every single patient compared. No correlation was established as in spite of high CEA productive tumors the levels of CEA concentrations in sera were found to be within normal as well as pathological range. Parallel to this study, CEA concentrations in sera and ascites of 37 patients were compared using the same method. While in malignant ascites the levels of CEA concentration were always high in the pathological range over 100 ng, the levels in sera were within normal limits in four out of seven patients. In ascites of 27 patients with liver cirrhosis CEA concentrations were always low to 30 ng/ml. It could be concluded that the reason for disproportion between carcinoembryonic antigen concentrations is highly productive malignant tissue and moderate, even normal values in sera still remains obscure and controversial. On the other hand it suggested that the estimation of CEA concentrations in ascitic fluid might be more useful for differentiating the malignant from nonmalignant ascites than CEA concentrations values in sera. (Author abstract) (7 Refs)

17. THE IMPORTANCE AND SIGNIFICANCE OF CARCINOEMBRYONIC ANTIGEN (CEA) IN THE MONITORING OF CANCER AND EVALUATION OF ITS TREATMENT.

Mauri S, Tagliabue P, Margara C, Bellan L
Divisione di Medicina Geriatrica, Ospedale S. Andrea, Vercelli, Italy
Minerva Med; 73(11):589-592 1982

Evaluation of carcinoembryonic antigen (CEA) was performed in 377 patients, 250 of them had tumors and 127 non-neoplastic diseases. Of 127 non-oncologic patients, 78 had normal values, 44 showed slight change, and 5 had significantly increased CEA values, two of them had progressive hepatic disease and 3 had pronounced hepatic stasis. Of 250 oncologic patients, 72 had increased CEA values, and advanced cancer often with metastases. Normal values were found in 178 patients, and in 5 of them CEA values increased with spreading and advancement of the disease. Most patients with increased CEA values had cancer of intestine, lung, liver, and stomach. Patients with thyroid cancer had normal CEA values. Chemotherapy was administered to 26 patients. CEA values were determined before, during, and after therapy. In 13 patients CEA values were reduced, size of tumor was decreased, and patients felt better subjectively. In some patients increase in CEA values indicated appearance of metastases long before clinical symptoms. CEA values were of little use in diagnosis of cancer, but proved more useful in monitoring the treatment and evolution of the disease. (17 Refs) (In ITA)

18. INDICATIONS FOR SURGICAL TREATMENT OF RECURRENT COLORECTAL NEOPLASMS AND THEIR METASTASES.

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Helv Chir Acta; 48(6):873-878 1982

Surgical treatment of recurrences of colorectal neoplasms (CRN) detected due to elevated blood carcinoembryonic antigen (CEA) levels and of pulmonary and hepatic metastases is discussed. Results of surgical treatment of CRN recurrences and metastases have been poor due to late presentation and nonspecificity of symptoms. Prior to surgery, measurement of CEA levels is of little diagnostic importance in CRN due to its lack of specificity. Following surgery, increases in CEA levels are indicative of CRN recurrence. In CRN patients with preoperative elevation of CEA, absence of postoperative decrease is associated with a poor prognosis. The mean survival for patients with liver metastases of CRN is 8 mo, although it is doubled in the case of solitary metastases. No evidence exists to suggest that surgical treatment of the CRN liver metastases significantly prolongs survival. Pulmonary metastases of CRN usually occur in later stages and rarely are isolated, usually accompanied by local recurrence, liver metastases, and other sites of involvement. (21 Refs) (In FRE)

19. TUMOR MARKERS IN CARCINOMA AND PREMALIGNANT STATES OF THE STOMACH IN HUMANS.

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Dept. Pathology, Flinders Univ. South Australia, Bedford Park 5042, Australia
Eur J Cancer Clin Oncol; 18(3):227-235 1982

Tissue sections taken from areas of carcinoma, areas of intestinal metaplasia in stomachs bearing carcinoma and areas of intestinal metaplasia in stomachs showing atrophic gastritis only were examined for eight markers: a tumor-derived colon-specific antigen (tCSA), carcinoembryonic antigen (CEA), alpha-fetoprotein (AFP), pregnancy-specific beta-glycoprotein 1 (SP1), human placental lactogen (HPL), human beta chorionic gonadotrophin (beta-HCG), transferrin (TF) and ferritin (FE). In terms of the number of markers demonstrated in each of the three categories, there is a close similarity between the cells of adenocarcinoma and cells of intestinal metaplasia in cases of cancer, but not to similar metaplastic cells in atrophic gastritis cases. In addition, it appears that the presence of tCSA and SP1 is closely linked to carcinoma, though only approx half of such cases contain these markers. It would also appear that there are two types of morphologically identical intestinal metaplasia, one related to cancer, the other not. No difference was found between so-called intestinal type and diffuse type carcinomas. (Author abstract) (28 Refs)

20. SERUM LEVELS OF CARCINOEMBRYONIC ANTIGEN AND A TUMOR-EXTRACTED CARCINOEMBRYONIC ANTIGEN-RELATED ANTIGEN IN CANCER PATIENTS.

Shively JE, Spayth V, Chang FF, Metter GE, Klein L, Present CA, Todd CW

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Cancer Res; 42(6):2506-2513 1982

Levels of carcinoembryonic antigen (CEA) and a tumor-extracted CEA-related antigen (TEX) were determined in sera from patients with carcinomas of the breast, colon, lung, head and neck, and a number of miscellaneous categories. The purpose of this study was to compare the levels of each antigen at various stages of malignant disease. Competitive radioimmunoassays developed in our laboratory were shown to be sufficiently specific to detect either of these two antigens independent of each other. The results indicate that: (a) with our specific assays, CEA was not significantly elevated in smoker controls, but TEX was elevated in 29% of smoker controls; (b) TEX was equivalent to CEA as a tumor marker for colonic cancer. TEX was better than CEA as a marker for lung cancer and, based on limited data, there is a possibility that TEX is a significantly better tumor marker than is CEA in early lung cancer; (c) TEX was superior to CEA as a tumor marker for breast and head and neck cancers; (d) there is a strong indication that serial determinations of TEX can be used as effectively as CEA in the monitoring of disease progress. These preliminary results must be confirmed by increasing the number of cancer patients and including nonmalignant disease controls. (Author abstract) (18 Refs)

21. PATHOMORPHOLOGICAL ASSESSMENT OF THE UTILITY OF RADIOIMMUNOLOGICAL TESTS OF THE CARCINOEMBRYONIC ANTIGEN AND ALPHA-FETOPROTEIN IN THE CLINICAL MANAGEMENT OF CANCER OF THE LARGE INTESTINE.

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Patol Pol; 32(3):329-339 1981

The serum carcinoembryonic antigen (CEA) and alpha-fetoprotein (AFP) levels were determined in 75 patients with carcinoma of the large intestine before surgery and in 28 of them also after surgery during a 2-yr follow-up period. Adenocarcinoma was diagnosed in 68 patients, mucinous carcinoma in 6 and mucocellular carcinoma in 1. The CEA levels measured before surgery av 2 nanog (ng)/ml in the patients in Dukes' Stage A, 19 ng/ml in Stage B and 93 ng/ml in C. The difference between the levels in Stages B and C was statistically significant. The follow-up examinations showed low CEA levels to be correlated with favorable prognosis in Stage A and with unfavorable course in Stage C. High CEA levels were found mostly in patients with well-differentiated adenocarcinomas and low levels mostly in those with adenocarcinomas of intermediate and low degrees of differentiation. High CEA levels were seen in patients with neoplasms with extensive necrosis. The AFP levels were elevated in 5/75 patients only before surgery, and they did not correlated with the advancement and histological structure of the tumors. (25 Refs) (In POL)

22. SERIAL CEA ASSAYS AND LIVER SCINTIGRAPHY FOR THE DETECTION OF HEPATIC METASTASES FROM COLORECTAL CARCINOMA.

Szymendera JJ, Wilczynska JE, Nowacki MP, Kaminska JA, Szawlowski AW

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Dis Colon Rectum; 25(3):191-197 1982

Of 340 patients with histologically proven colorectal carcinoma, hepatic metastases were diagnosed in 90 (26%), in 50 at the time of initial surgery (synchronously) and in 40 during the postoperative follow-up (metachronously). At the time of initial surgery, plasma carcinoembryonic antigen (CEA) levels were markedly elevated in patients with synchronous metastases and normal or only moderately elevated in those with metachronous metastases. During follow-up, CEA levels in the entire group of patients with metastases remained normal in 8% and rose in the remainder: very quickly in 85% and slowly in 15%. Hepatic metastases were diagnosed by strict scintigraphic criteria in 70% of patients and were suggested by liberal criteria in the remainder. During follow-up, hepatic metastases progressed in the scintigraphic image from those defined by liberal to those diagnosed by strict criteria. In two-thirds of the patients, liver scintigraphy proved to be superior to the CEA test in diagnosing hepatic metastases by strict criteria; in the majority of the remainder of patients, the CEA test, particularly in cases with a pattern of fast increase of CEA in plasma, suggested metastases before a definite diagnosis could be made by liver scintigraphy. In only 3% of the patients neither liver scintigraphy nor the CEA test were indicative of metastases. Thus, the two diagnostic modalities, when combined, could attain a sensitivity of 97%, when patients with persistently rising CEA levels and concomitant liver lesions defined by the liberal criteria were grouped with those for whom scintigraphy was unequivocal. (Author abstract) (34 Refs)

23. THE PRESENCE OF ONCOFOETAL ANTIGENS IN LARGE BOWEL CARCINOMA.

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Aust NZ J Surg; 52(1):30-34 1982

This paper is an immunohistological study of the occurrence of the oncofetal antigens, carcinoembryonic antigen (CEA), small intestine mucin antigen (SIMA), and normal large bowel mucin antigen (LIMA) in 60 surgically resected colons: 10 non-malignant specimens and 50 colorectal carcinomas. SIMA is a new oncofetal antigen found in mucinous carcinoma of the large bowel. In the adult it is normally present only in the duodenum and jejunum. Of the 50 carcinoma specimens, 13 were mucinous, 17 non-mucinous and 20 mixed mucinous and non-mucinous. LIMA was the only antigen detected in the mucosa of non-malignant specimens. In mucinous carcinomas only SIMA was present, whilst in the non-mucinous specimens CEA was always found and to a lesser extent LIMA. The same relationship was observed in mixed tumors: SIMA in mucinous and CEA-LIMA in the non-mucinous parts. In the mucosa adjacent to the cancer in all 50 cases there was evidence of an increase or decrease in LIMA. In 42 cases (84%) both oncofetal antigens (CEA and SIMA) could also be detected in this transitional or perineoplastic epithelium at varying distances from the tumor. These results provide evidence to suggest that the majority of large bowel carcinomas occur in areas of metaplastic change. (Author abstract) (23 Refs)

24. EFFICIENT FOLLOW-UP OF PATIENTS SUBJECTED TO RADICAL SURGERY FOR COLORECTAL CANCER.

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Tidsskr Nor Laegeforen; 102(5):305-308 1982

Efficient follow-up of patients subjected to colorectal carcinoma is proposed. Approx 1,100 new cases of colon cancer and 580 new cases of rectal cancer are diagnosed annually in Norway. Approx 2/3 of all patients with cplorectal carcinoma can be operated on with curative intent. One third of the patients subjected to radical surgery develop recurrences during the first yr, and another 10% during the second yr. Approx 50% of all patients die within 1 yr after diagnosis. Local recurrences in or near anastomoses occur in 10.5% of all patients, synchronous cancer in 2.5-5%, metachronous cancer in 3.5% of all patients subjected to surgery, and precancerous polyps can exist in a segment of the colon or rectum which has not been resected. To rule out synchronous cancer to detect recurrences in the anastomosis, and to detect metachronous cancer and precancerous states, the patients subjected to radical surgery should be examined by coloscopy and colon x-ray in the first 3 mo after surgery, then after 9-12 mo. If no polyps or precancerous conditions are found, further coloscopy, or rectoscopy, or colon x-ray should be performed for special indications only. The carcinoembryonic antigen levels should be determined in patients subjected to radical surgery every 3 mo during the first yr and every 6 mo during the second. Routine follow-up of patients subjected to radical surgery for colorectal cancer beyond the first 2 yr after surgery seems to be of little value. (15 Refs) (In NOR)

25. TUMOR ASSOCIATED PRODUCTS IN COLONIC LAVAGE FLUID.

Vellacott KD, Groom G, Balfour TW, Baldwin RW, Hardcastle JD
Dept. Surgery and Cancer Res. Campaign Lab., Univ. Nottingham, University Park, Nottingham NG7 2RD, England
Clin Oncol; 8(1):61-67 1982

Colonic lavage techniques have been used to look for tumor associated products in 132 patients. Carcinoembryonic antigen estimations on 83 showed higher levels in those with adenomatous polyps greater than 1 cm diameter, colonic cancers and inflammatory bowel disease than in those with no evidence of gastrointestinal pathology. Enzyme studies showed beta-glucosidase was elevated in similar groups. Using a modified C1q binding assay no difference in levels of immune complexes between the diagnostic groups was found. Carcinoembryonic antigen and glycolytic enzymes in feces may prove useful for the diagnosis of early colorectal tumors in asymptomatic screening studies. (Author abstract) (16 Refs)

26. EXTRACORPOREAL IMMUNOADSORPTION OF PLASMA FROM A METASTATIC COLON CARCINOMA PATIENT BY PROTEIN A-CONTAINING NONVIABLE STAPHYLOCOCCUS AUREUS: CLINICAL, BIOLOGICAL, SEROLOGIC, AND HISTOLOGIC EVALUATION OF THE PATIENT'S RESPONSE.

Ray PK, Idiculla A, Mark R, Rhoads JE, Thomas H, Bassett JG, Cooper DR
Dept. Surgery and Microbiology, Medical Coll. Pennsylvania and Hosp., Philadelphia, PA, 19129
Cancer; 49(9):1800-1809 1982

A patient with a metastatic colon carcinoma was treated by immunoadsorption (IA) therapy using heat-kiled, formalin-stabilized protein A-containing Staphylococcus aureus Cowan I as the immunoadsorbent. The patient experienced both subjective and objective positive clinical response without undue morbidity. The patient's response correlated with the laboratory findings of decreased concentrations of carcinoembryonic antigen (CEA), immunoglobulin G (IgG), immune complexes (IC) and histopathologic data. The patient underwent surgery following 15 IA treatments; she lived for 18 mo post-treatment. (Author abstract) (50 Refs)

27. SCIRRHOUS ARGYROPHIL CELL CARCINOMA OF THE STOMACH WITH MULTIPLE PRODUCTION OF POLYPEPTIDE HORMONES, AMINE, CEA, LYSOZYME, AND HCG.

Tahara E, Ito H, Nakagami K, Shimamato F, Yamamoto M, Sumii K
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Cancer; 49(9):1904-1915 1982

Sixteen argyrophil cell carcinomas in 59 gastric scirrhous carcinomas were examined histologically, ultrastructurally, and immunohistochemically for polypeptide hormones, CEA, lysozyme, and HCG. In 9 of these 16 tumors, polypeptides such as gastrin, somatostatin, and glucagon were demonstrated. Six of these nine tumors contained all three hormones, and three of these six tumors also had argentaffin cells. In all of these 16 tumors CEA were observed. Eight of them had CEA, lysozyme, and acid mucin synchronously. Of the above six tumors containing three peptides, three produced focal HCG. Ultrastructurally, several types of secretory granules were noted. Histologically, these 16 tumors showed poorly differentiated adenocarcinomas or signet ring cell carcinomas. Macroscopically, generalized type was 11 and localized type 5. No hormonal syndrome was detected in any of the patients. It was suggested that these scirrhous argyrophil cell carcinomas of the stomach with the multifunction originate from totipotent immature cells of endodermal origin. (Author abstract) (46 Refs)

28. THE ROLE OF TENNESSEE ANTIGEN IN THE DIAGNOSIS OF GASTROINTESTINAL MALIGNANCY.

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Aust NZ J Surg; 52(1):39-41 1982

Tennessee antigen (TAG) is a glycoprotein which has been extracted from adenocarcinoma of the colon. It is one of the numerous tumor associated antigens which has been developed and there is evidence that it differs considerably from carcinoembryonic antigen (CEA) preparations. A commercial kit using a hemagglutination inhibition assay is available and its ability to discriminate between benign and malignant conditions of the gastrointestinal tract has been studied, using 7.7 units/ml as the upper limit of normal. With upper gastrointestinal disease, discrimination is comparable to that achieved with TAG by other workers and also to that achieved with CEA. For gastric carcinoma TAG has a sensitivity of 71% and a specificity of 77%. With lower gastrointestinal tract disease discrimination was poor, TAG having a sensitivity of 76% but a specificity of 44% for colorectal carcinoma. Discrimination between pancreatic carcinoma and chronic pancreatitis was poor, TAG having a sensitivity of 100% for carcinoma and a specificity of 22%. (Author abstract) (8 Refs)

29. TISSUE POLYPEPTIDE ANTIGEN - A NEW TUMOUR MARKER?

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Aust NZ J Surg; 52(1):41-43 1982

The possibility of using Tissue Polypeptide Antigen (TPA) as a tumor marker in the diagnosis and follow-up of patients with malignant tumors was reported. We have taken up these suggestions and examined the possible role of TPA as a tumor marker in gastric and colo-rectal carcinoma. TPA and CEA (Carcinoembryonic Antigen) values were determined in 39 patients with gastric and 60 patients with colo-rectal carcinoma. The tumors were histologically proven. The histological classification of the gastric carcinomas was carried out according to the recommendations of the AJC (American Joint Committee for cancer staging and end results reporting) and that of the colo-rectal carcinomas was according to Dukes. Fifty-two surgical patients with benign diseases were used as controls. In this group the incidence of false positive values was 15.3% for TPA and 23% for CEA. In gastric carcinoma 30 out of 39 patients (76.9%) had on elevated TPA level (medium 275.4 n/l), in contrast CEA was elevated in 18 out of 35 patients (46.1%, medium 24.6 ng/ml). In colo-rectal cancer the TPA level was increased in 61.6% ie 37 out of 60 patients (medium 260.2 n/l). Elevated CEA levels were detected in 38 out of 60 patients (63.6%, medium 192 ng/ml). The mean values of TPA and CEA rise with advancing tumor stages. Elevated TPA levels were also found in non malignant diseases. Possible sources of error are inflammatory reactions. Therefore increased TPA values should be considered indicative of neoplasia only if infections or inflammatory diseases can be excluded and the first value is confirmed by repeated examination. The high incidence of increased values in early tumor stages (Dukes A or AJC 1), seems to justify the inclusion of tests for these antigens into the diagnostic and follow-up routine of gastric and colorectal cancer. (Author abstract) (9 Refs)

30. TISSUE CARCINOEMBRYONIC ANTIGEN, DYSPLASIA, AND DISEASE DURATION IN COLONIC INFLAMMATORY BOWEL DISEASE.

Greenstein AJ, Panvelliwalla DK, Katz LB, Heimann TM, Donnelly J, Pertsimlidis D, Geller S, Smith H, Aufses AH

Dept. Surgery, Mount Sinai Sch. Medicine City Univ. New York, New York, NY

Am J Gastroenterol; 77(4):212-215 1982

Tissue carcinoembryonic antigen (CEA) was studied in five groups of patients: 8 ulcerative colitis patients with mild or no dysplasia, 5 ulcerative colitis patients with severe dysplasia, 7 Crohn's disease patients with nondiseased colon, 9 Crohn's disease patients with diseased colon, and 18 colorectal cancer patients from the noncancerous colon resection margins. CEA levels were significantly lower in the normal colon Crohn's group than all other groups (p less than 0.05). CEA levels were significantly higher in the severe dysplasia ulcerative colitis group than all other groups (p less than 0.05). The Crohn's disease patients with diseased colon, the ulcerative colitis patients with mild or no dysplasia, and the colorectal cancer group with noncancerous colon all had similar intermediate CEA levels. (Author abstract) (26 Refs)

31. ROLE OF IMMUNOLOGICAL TESTS IN DIFFERENTIAL DIAGNOSIS OF PANCREATITIS AND CANCER OF THE PANCREAS.

Vel'bri SK, Khiarmat KhL
Dept. Clinical Oncology, Inst. Experimental and Clinical Medicine, Tailin, USSR
Ter Arkh; 54(2):52-55 1982

Diagnostic efficacy of immunological tests was studied in 51 patients with pancreatitis and 48 patients with Stage II-IV pancreatic cancer. Carcinoembryonic antigen (CEA) levels of greater than 40 nanog/ml were observed in 25/48 patients with pancreatic cancer and only in 4/51 patients with pancreatitis. Av concentration of CEA was 25.4 nanog/ml in the patients with pancreatitis and 81.3 nanog/ml in the patients with pancreatic cancer. The highest CEA levels (134.4 nanog/ml) were observed in the patients with liver metastases. Immunodiffusion technic showed the presence of alpha-fetoprotein in the blood sera of two patients with Stage III cancer of the pancreas. Common pancreatic antigen was present in the blood sera of 60% of cancer patients and of 27% of pancreatitis patients. Sensitization of lymphocytes to the pancreatic tissue was observed in 33% of cancer patients and in 50% of pancreatitis patients. Index of lymphocyte blast-transformation in the cancer patients was significantly lower than that in pancreatitis patients (30.8% and 42.6%, respectively). It was concluded that the use of several immunological tests can enhance the differential diagnosis between pancreatitis and cancer of the pancreas. (16 Refs) (In RUS)

32. DIAGNOSIS OF CARCINOMA OF THE PANCREAS BY ASSAY OF IMMUNOSUPPRESSIVE ACIDIC PROTEIN.

Matsuno S, Kobari M, Matsuda Y, Sato T
First Dept. Surgery, Tohuku Univ. Sch. Medicine, Sendai 980, Japan
Tohoku J Exp Med; 136(1):1-10 1982

Immunosuppressive acidic protein (IAP) was measured by single radial immunodiffusion in serum from 46 pancreatic cancer patients, 211 controls, and patients with other malignant or benign inflammatory pancreatic diseases. A normal value of serum IAP of less than 500 ug/ml was used because 194/211 (91.9%) of the controls were below this value. Elevated serum IAP levels were seen in 44/46 (96%) pancreatic cancer patients, 24/26 (92%) bile duct cancer patients, all duodenal papilla or gallbladder cancer patients, 19/29 (66%) of chronic pancreatitis patients, all of acute pancreatitis or pancreatic cyst patients, and 0/3 insulinoma patients. Serum IAP correlated with tumor size and metastatic involvement of the liver and peritoneum, but not infiltration of the pancreatic capsule. It also seemed to correlate with recurrence after surgery, but not with serum carcinoembryonic antigen (CEA) levels, which were elevated (greater than 2.5 nanog/ml) in only 26/46 (57%). Portal blood sampling in four patients did not show elevated IAP or CEA levels at the site of tumor. The value of this assay for screening for pancreatic cancer is discussed. (10 Refs)

33. HEPATOCELLULAR CARCINOMA IN RURAL SOUTHERN AFRICAN BLACKS.

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Dept. Medicine, Univ. Witwatersrand Medical Sch., Hospital Hill, Johannesburg 2001, South Africa
Medicine (Baltimore); 61(2):98-108 1982

The clinical presentation and natural history of hepatocellular carcinoma, as well as its association with cirrhosis and the hepatitis-B virus surface antigen, were studied in 585 Black males living in rural areas of southern Africa. In addition, the value of serum alpha-fetoprotein concentrations, serum biochemical changes, and various radiologic, isotopic and sonographic techniques in the diagnosis of hepatocellular carcinoma in this population was reviewed. The mean age of the patients was 35 yr and 40% of them were less than 30 yr of age. The most common presenting complaints were upper abdominal pain, swelling of the abdomen, wt loss and weakness. Rupture of the tumor with acute intraperitoneal hemorrhage occurred in 10% of the patients. The liver was almost always enlarged and focal tenderness was usual. An arterial bruit was heard over the liver in 23% of the patients. Ascites and splenomegaly were each present in about one-half of the patients, and 28% were jaundiced. Progressive muscle wasting was almost invariable. The tumor was rarely resectable and the patients did not respond to radiation therapy or cancer chemotherapy: the mean survival from the onset of symptoms was 11.1 wk and from the time of diagnosis 6 wk. Macronodular cirrhosis was present in the non-tumorous liver tissue at necropsy in 60% of the patients. The hepatitis-B surface antigen was detected in the serum of 62% of the patients. It was more common in younger patients, but was not related to the presence of alpha-fetoprotein. HBs antigenemia was equally common in patients with and without cirrhosis. Alpha-fetoprotein was present in high concentration in the serum of 67% of the patients and provided an excellent indicator of the diagnosis of hepatocellular carcinoma. It was more commonly found in younger patients. Biochemical changes were non-specific and did not differentiate hepatocellular carcinoma from cirrhosis or other mass lesions in the liver. Chest radiographs showed elevation of the right hemidiaphragm in 30% of the patients and multiple pulmonary metastases in 25%. One or more defects were invariably seen on isotope liver scans but the picture was not diagnostic of hepatocellular carcinoma. Blood flow scintigraphy usually showed the lesions to be vascular. Echogenic or partly echogenic and partly anechoic lesions with ill-defined edges were demonstrated on ultrasonography. Computerized axial tomograms and hepatic arteriography were useful in assessing the extent of the tumor in relation to possible resection. (Author abstract) (28 Refs)

34. HEPATITIS B ANTIGEN IN SERUM OF THE PATIENTS WITH CHRONIC LIVER DISEASES AND MALIGNANT HEPATOMA.

Libman E, Stojsic S, Marton B, Lemberger J

Sluzba za internisticke bolesti, Interno odeljenje, Medicinski centar, Subotica, Subotica, Yugoslavia

Med Pregl; 34(9/10):389-392 1981

Serum radioimmunoassay (RIA) was used for the determination of hepatitis B surface antigen (HBsAg). Serum of 30 healthy controls (HC), of 50 blood donors (BD: 20-54 yr old), of 96 patients with chronic persistent hepatitis (CPH), of 8 with aggressive hepatitis (AH), of 95 with alcoholic hepatic cirrhosis (AHC), of 10 with postnecrotic hepatic cirrhosis (PHC), and of 20 with malignant hepatoma (MH) was analyzed for HBsAg. RIA was also used for the determination of alpha-fetoprotein (AFP). Increased values of HBsAg were observed in 6 of the BD, in 22 of the patients with CPH, in 5 with AH, in 4 with AHC, in 3 with PHC, and in 1 with MH. Increased values of AFP were found in 2 patients with AH, in 6 with AHC, in 6 with PHC, and in 14 with MH. Concentrations of AFP were 18-11,812 nanog/ml in patients with MH. One patient with primary MH and increased value of HBsAg, did not have increased value of AFP. (28 Refs) (In SCR)

35. A CLINICAL EVALUATION OF SERUM ALPHA-1-ANTICHYMOTRYPSIN LEVELS IN LIVER DISEASE AND CANCERS.

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Gastroenterol Jpn; 16(6):582-591 1981

The serum levels of alpha-1-antichymotrypsin (ACT) were studied in 168 patients with various liver diseases and cancers in conjunction with other liver function tests, serum sialic acid, AFP and CEA. The ACT levels in acute viral hepatitis and chronic hepatitis were not significantly altered compared with the normal level (220 +-40 ug/ml), although the level was slightly increased or decreased temporarily during the acute phase of the former. In liver cirrhosis, the mean level was significantly lower than the normal in spite of the absence of signs of hepatic decompensation (168 +-51 ug/ml, p less than 0.001). In contrast to cirrhosis, the levels were increased to various extents in 65% of cases with hepatoma, in spite of the association of liver cirrhosis in the majority of them. Much higher levels were observed in all cases of metastatic liver cancers and cancers of the pancreas and the biliary tract. The elevations were observed even in cases without the increase of AFP or CEA. Both in cirrhosis and cancers, ACT levels were not correlated with any of serum bilirubin and serum enzyme activities, but were positively correlated with the levels of plasma fibrinogen and serum sialic acid. The measurement of serum ACT level can be taken advantage of for the diagnosis and monitoring of liver cirrhosis and liver cancers, particularly of hepatoma without AFP elevation. (Author abstract) (18 Rets)

36. PROSPECTIVE EVALUATION OF DIAGNOSTIC PROCEDURES IN PATIENTS SUSPICIOUS OF MALIGNANT HEPATOMEGALY.

Moreno J, Uribe M, Pena A F, Elizondo J, Gallo S, Hernandez O J, Quiroz F F, Nieto L

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Rev Invest Clin; 33(4):343-348 1981

Forty-five patients (16 men, 29 women; 16-88 yr old) with clinical hepatomegaly (HM) or epigastric tumor associated with three of the following factors: decline in general state of health, loss of greater than 5 kg of body wt without diuretics, decompensation of stable hepatic cirrhosis, recent appearance of abdominal pain, or fever of undetermined origin were selected for the study. Final diagnosis was established by laparoscopy and biopsy in 34 of the patients, and by laparotomy in 11. Eleven of the patients had primary hepatic carcinoma, 18 had metastatic carcinoma, and others had benign hepatic changes, which were associated in 4 with extrahepatic cancer. Alkaline phosphatase (AP), alpha-fetoprotein (AFP), carcinoembryonic antigen (CEA), liver gammagraphy with 99mTc2S7 (LS), ultrasonography (US), hepatic angiography (ANG), and laparoscopy (LAP) were performed in 21-89% of the patients. AP was sensitive in 75% of the patients and specific in 65%; AFP was sensitive in 17% and specific 88%; CEA was sensitive in 36% and specific in 92%; LS showed filling defect with sensitivity and specificity in 86%, US was sensitive in 87% and specific in 82%, and ANG was sensitive and specific in all the patients tested. AFP and CEA were of little use in the diagnosis of hepatic cancer. US and LS were equivalent in indicating hepatic masses. Only one patient showed side effect (severe reaction to contrast medium) during ANG. (18 Refs) (In SPA)

37. ALPHA-FETOPROTEIN AND CARCINOEMBRYONIC ANTIGEN IN PANCREATOBILIARY DISEASE WITH AND WITHOUT JAUNDICE.

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J Surg Oncol; 19(4):228-232 1982

A comparative study of alpha-fetoprotein (AFP) and carcinoembryonic antigen (CEA) in serum was made by radioimmunoassay in 66 patients with pancreatobiliary disease with and without obstructive jaundice, biliary concentrations of these proteins were assayed in 12 patients with benign and 7 patients with malignant disease. There was no statistical difference in serum AFP between these two groups but there was a difference in serum CEA. Although CEA and AFP in bile in both groups were higher than in serum there was no statistical difference in serum CEA and AFP in patients with and without obstructive jaundice in either benign or malignant disease. In benign disease, patients with inflammation had higher serum CEA than normal. Although there was no statistical difference in serum CEA in patients with and without liver metastases, the serum CEA in liver metastases was significantly higher than in benign disease. We concluded that AFP is unlikely to be important in the assessment or management of patients with cancers other than those derived from the liver or yolk sac, and that the elevation of serum CEA in patients with malignant pancreatobiliary disease either with or without obstructive jaundice occurs mainly in the presence of widespread malignancy, especially in liver metastases. (Author abstract) (5 Refs)

38. THOROTRAST-INDUCED HEPATIC ANGIOSARCOMA, AND COMBINED HEPATOCELLULAR AND CHOLANGIOCARCINOMA IN A SINGLE PATIENT.

Kojiro M, Kawano Y, Kawasaki H, Nakashima T, Ikezaki H
First Dept. Pathology, Kurume Univ. Sch. Medicine, Kurume, 830, Japan
Cancer; 49(10):2161-2164 1982

A 64-yr-old man developed hepatic angiosarcoma, and combined hepatocellular and cholangiocarcinoma, 36 yr after Thorotrast administration. The patient presented with a large mass in the right upper quadrant. His serum alpha-fetoprotein increased from 800 ng/ml to 51.2 ug/ml, and liver biopsy disclosed hepatocellular carcinoma. At autopsy, the liver had two different malignant neoplasms; angiosarcoma and combined hepatocellular and cholangiocarcinoma. Metastases of angiosarcoma to both lungs and of cholangiocarcinoma to periaortic lymph nodes were also seen. Interestingly, some neoplastic cells of angiosarcoma exhibited globular hyaline inclusions, which were Periodic-Acid-Schiff reaction positive and diastase-resistant. (Author abstract) (13 Refs)

39. THE DETECTION AND MEASUREMENT OF ONCODEVELOPMENTAL PROTEINS IN GYNECOLOGICAL MALIGNANT DISEASE.

Cerni C, Tatra G
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Arch Gynecol; 231(2):159-165 1981

The correlation of oncodevelopmental antigens with the existence and clinical course of gynecologic malignancies is discussed. Alpha-fetoprotein (AFP) relates to progression of teratocarcinomas, usually with yolk sac elements, and can be used during therapy for control and management. Carcinoembryonic antigen (CEA) is elevated to varying degrees in gynecologic malignancies, but does not appear to correlate with the clinical course of the disease. Alpha2-pregnancy-associated globulin (alpha2-PAG) was reported to have a 60% correlation with clinical course in one study, but the authors found only a 38.1% correlation in 126 gynecologic malignancies. Human chorionic gonadotropin (HCG) correlates well with the course of germ cell tumors, but not other non-trophoblastic gynecologic tumors. Human placental lactogen (HPL) is found in low concentrations in ovarian carcinoma patients, but does not correlate with the clinical state of the disease. Pregnancy-specific beta1-glycoprotein (SP-1) gives variable results, but serum levels do not appear to consistently correlate with disease. (47 Refs)

40. CARCINOEMBRYONIC ANTIGEN SERUM LEVELS IN PATIENTS WITH SQUAMOUS CELL CARCINOMA OF THE UTERINE CERVIX: CLINICAL SIGNIFICANCE.

te Velde ER, Persijn JP, Ballieux RE, Faber J
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Cancer; 49(9):1866-1873 1982

In 114 patients with invasive cervical cancer of the squamous cell type pretreatment CEA levels were determined. An individual upper limit of the normal range was derived taking into account the smoking habits and the age of each patient. Pretreatment CEA levels exceeding the upper limit of normal concurred with a very poor prognosis, regardless of the stage of the tumor. Moreover, in 92 patients longitudinal CEA patterns were established. The median follow-up time of the nonrecurrence patients was 4 yr. Three patterns appeared to be exclusively associated with the presence of recurrent cancer. The median lead-time obtained in patients demonstrating such patterns, was 13 wk. The clinical value and the possible therapeutic consequences of the findings presented are discussed in relation to the available knowledge of tumor growth in cervical cancer. (Author abstract) (39 Refs)

41. DIAGNOSTIC SIGNIFICANCE OF PREGNANCY-ASSOCIATED ALPHA2-GLYCOPROTEIN IN PATIENTS WITH OVARIAN CANCER.

Sawada M, Shimizu Y, Okudaira Y, Matsui Y, Nishiura H, Hayakawa K
Div. Gynecology, Dept. Clinical Res., Res. Inst. Microbial Diseases, Osaka Univ., Yamada-kami, Suita-City, Osaka, Japan
Gynecol Oncol; 13(2):229-236 1982

Pregnancy-associated alpha2-glycoprotein (alpha2-PAG) levels were measured in several kinds of samples by a modification of Laurell's electroimmunoassay using a rabbit anti-alpha2-PAG serum. Samples were sera obtained from healthy females (46 cases), patients with benign ovarian tumors (8 cases), patients with ovarian cancers (18 cases), nude mice bearing heterotransplanted human ovarian cancers (4 cases), and ascites and urine of cancer patients. Serum alpha2-PAG levels in patients with benign ovarian tumors were 3.8 +-3.2 U/ul and almost the same as those of controls (2.6 +-3.0 U/ul). However, serum alpha2-PAG levels were higher in patients with ovarian cancers (12.0 +-3.7 U/ul). alpha2-PAG was scarcely detected in ascites or urine obtained from cancer patients, and was not detected in sera of tumor-bearing nude mice, despite the high levels of alpha2-PAG in those of original patients. The reliability of alpha2-PAG as a tumor-associated marker in patients with ovarian cancer was reinforced by the comparison of the positive rates of the two parameters, alpha2-PAG and carcinoembryonic antigen (CEA). (Author abstract) (26 Refs)

42. SIMPLIFIED CEA RADIOIMMUNOASSAY IN THE FOLLOW-UP OF GYNECOLOGIC PATIENTS WITH TUMOR.

Horst M, Wiest W
Institut fur Klinische Radiologie, Klinikum Mannheim der Universitat Heidelberg, Theodor-Kutzer-Ufer, 6800 Mannheim 1, W. Germany
Fortschr Med; 100(11):482-483 1982

A new modified and simplified carcinoembryonic antigen (CEA) radioimmunoassay (RIA) was used in the follow-up of 50 gynecologic patients. Histologic diagnosis included 14 patients with cervical carcinoma (CA), 16 with CA of the uterine body, and 20 with ovarian CA. Study lasted from 14 days up to 1 yr including patients receiving radiotherapy and cytostatics. The values found for the CEA with RIA were 1.8-14.5 nanog (ng)/ml compared to the normal values of less than 2.5 ng/ml. Of eight control patients only one had the CEA 2.8 ng/ml, and all the others were less than 2.5 ng/ml. Increased values of CEA were observed in 56.3% of the patients with CA of the uterine body, in 78.6% with cervical CA and in 90% with ovarian CA. These values were in the same range as observed with the previous CEA RIA. Sharp increase was observed in some patients shortly before death. The new procedure is simpler, and the readings can be obtained within 4-6 hr. (In GER)

43. ENDODERMAL SINUS TUMOUR OF THE OVARY: THE PLACE OF ALPHAFETOPROTEIN DETECTION, SURGERY AND CHEMOTHERAPY.

Khoo SK, Buntine DW, Massay PF, Jones IS
Dept. Obstetrics and Gynaecology, Univ. Queensland, Brisbane, Australia
Aust NZ J Obstet Gynaecol; 21(4):217-225 1981

Two white females 36 (A) and 34 (B) yr old were treated by CHAMOA chemotherapy after an assay of a unilateral salpingo-oophorectomy revealing an endodermal sinus tumor. Progress was followed by weekly serum alphafetoprotein (AFP) assay. The chemotherapy consisted of four monthly 9-day courses of hydroxyurea, vincristine, methotrexate, citrovorum factor, cyclophosphamide, and adriamycin D. Case A has been in remission over 2 yr after a 2nd laparotomy and total hysterectomy 8 mo after presentation. Case B developed metastases to the peritoneum, omentum, and para-aortic nodes shortly after the last course. After total hysterectomy, chemotherapy consisted of four monthly 15-day courses of vinblastine, bleomycin, and cis-diaminedichloroplatinum. This subject has also been in remission for 2 yr. In both cases the AFP became undetectable during the 1st or 2nd CHAMOA course. In case B AFP rose rapidly after the 4th course and was the occasion for the discovery of the metastases on laparotomy. Reports of diagnosis, chemical and surgical treatment, and prognosis for this tumor are reviewed. Diagnosis should be restricted to immunohistochemical staining strongly positive only for AFP, and not for carcinoembryonic antigen or human chorionic gonadotrophin. (35 Refs)

44. MEDIASTINAL NONSEMINOMATOUS GERM CELL TUMORS: THE ROLE OF COMBINED MODALITY THERAPY.

Vogelzang NJ, Raghavan D, Anderson RW, Rosai J, Levitt SH, Kennedy BJ
Box 286 Mayo Memorial Building, 420 Delaware St., Minneapolis, MN, 55455
Ann Thorac Surg; 33(4):333-339 1982

Twelve male patients (14-34 yr old) with mediastinal nonseminomatous germ cell tumors were treated with chemotherapy (with or without surgery and radiotherapy) and the value of cisplatin-based chemotherapy was evaluated. Chemotherapy with cisplatin, vinblastine, and bleomycin (PVB) was administered to six patients every 3 wk. A seventh patient received PVB plus actinomycin D and cyclophosphamide (VAB-6). Nine patients received radiotherapy (3,000-6,000 rads). Evidence of local extension was seen in 10 patients. Of the five patients treated without cisplatin-based chemotherapy, two achieved a complete clinical remission with initial radiotherapy, two achieved complete remission with initial surgery, and one showed no response to initial chemotherapy. All these patients died within 1 yr of diagnosis except one patient who survived for 50+ mo. who was treated with a debulking operation, followed immediately by radiotherapy and adjuvant chemotherapy with vinblastine, bleomycin, and cyclophosphamide. Of the seven patients treated with cisplatin-based chemotherapy, no complete responses were noted, two patients achieved partial remission, two had no objective decrease in tumor size but had normalization of alpha-fetoprotein and human chorionic gonadotropin, and three showed no response. Four of these patients died within 12 mo of diagnosis. One of the partial responders who died was found to be free of tumor at autopsy. Tentative guidelines for treatment of patients with mediastinal nonseminomatous germ cell tumors are presented. (26 Refs)

45. TESTICULAR SEMINOMA: A REVIEW OF 30 CASES.

Laverdiere J
Centre d'onco-radiologie, Hotel-Dieu de Quebec, Pavillon Carlton-Auger, Quebec, Canada
Union Med Can; 110(10):905-906 1981

A retrospective analysis of 30 patients (20-58 yr old) with testicular seminomas (1 spermatocytic, 4 anaplastic, and 25 classic) treated with radiotherapy is presented. Lymphatic metastasis, particularly involving the para-aortic lymph nodes, and secondarily the iliac, supra-clavicular, and mediastinal lymph nodes, are most common. Diagnostic technics include lymphography, pyelography, tomography, and evaluation of diagnostic markers (alpha fetoproteins and beta subunit of human chorionic gonadotropin). Patients were classified as Stage I (18 patients), II (8), or III (4). Stage I patients were treated with cobalt60 radiotherapy (2,500 rad in 3 wk) to the para-aortic region. In Stage II patients, extra radiation (1,000-1,500 rads) also was delivered to known lymphatic masses along with prophylactic mediastinal and sub-clavicular radiotherapy (2,500 in 3 wk). Stage III treatment varied. The overall 3-and 5-yr recurrence-free survival rates for the 30 patients was 85% and 84%, respectively. Rates for Stage I patients were 92% and 91%, respectively. Rates for Stage II patients were 80% and 71%, respectively. In Stage II patients, recurrences usually observed in the abdomen and lungs were treated with radiotherapy and chemotherapy (alkylating agents and adriamycin). (no Refs) (In FRE)

46. HUMAN CHORIONIC GONADOTROPIN AS A MARKER FOR TESTICULAR TUMORS.

Mann K
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Fortschr Med; 100(9):379 1982

Potential tumor markers were investigated in serum samples obtained from 230 patients with testicular tumors. Human chorionic gonadotropin (HCG) and alpha-fetoprotein were elevated in the serum of patients with testicular malignancies. In addition, elevated levels of HCG alpha- and beta-chains were also detected. It is suggested that radioimmunoassays of HCG could be used in primary diagnosis of malignant testicular tumors, staging, and monitoring the course of the disease and the effects of therapy. (no Refs) (In GER)

47. CORRELATION OF SERUM TUMOR MARKERS AND LYMPHANGIOGRAPHY WITH DEGREES OF NODAL INVOLVEMENT IN SURGICAL STAGE II TESTIS CANCER.

Vugrin D, Whitmore WF, Nisselbaum J, Watson RC
Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
J Urol; 127(4):683-684 1982

There were 60 patients at our cancer center who underwent serum tumor marker studies (beta subunit of human chorionic gonadotropins and alpha-fetoprotein) and pedal lymphangiography before retroperitoneal lymph node dissection. Surgical stage II cases were divided according to tumor, node and metastasis staging. Beta-human chorionic gonadotropin and/or alpha-fetoprotein was elevated in 9% (1/11) of the N1 cases, 36% (5/14) of the N2A cases, 50% (13/26) of the N2B cases and 89% (8/9) of the N3 cases. Lymphangiography was positive or suspicious in 9% (1/11) of the N1 cases, 36% (5/14) of the N2A cases, 46% (12/26) of the N2B cases and 56% (5/9) of the N3 cases. Serum tumor markers and lymphangiography combined suggested lymph node metastases in 18% (2/11) of the N1 cases, 50% (7/14) of the N2A cases, 73% (19/26) of the N2B cases and 100% (9/9) of the N3 cases. We conclude that tumor markers and lymphangiography measurements are equally effective in the diagnosis of retroperitoneal lymph node metastases and that diagnostic accuracy is enhanced significantly by combining these 2 modalities. Retroperitoneal lymph node dissection remains the most reliable staging procedure. Reports on the accuracy of clinical staging should be correlated with subcategories of stage II disease. (Author abstract) (8 Refs)

48. ACCURACY OF PREOPERATIVE STAGING IN STAGES A AND B NONSEMINOMATOUS GERM CELL TESTIS TUMORS.

Rowland RG, Weisman D, Williams SD, Einhorn LH, Klatte EC, Donohue JP
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J Urol; 127(4):718-720 1982

Primary radical retroperitoneal lymphadenectomy currently is used for pathologic staging of nonseminomatous germ cell testis tumors unless advanced disease is present initially. Many attempts have been made for accurate staging of these tumors preoperatively. We reviewed the accuracy of alpha-fetoprotein and beta-human chorionic gonadotropin serum markers, and abdominal ultrasound and computerized tomography scans in preoperatively staging 64 patients with stage A or B nonseminomatous germ cell testis tumors seen at our university between 1977 and 1980. The results of the preoperative staging studies were correlated with the pathologic stages obtained by retroperitoneal lymphadenectomy. Over-all, the correct results were obtained in 61% of the patients with alpha-fetoprotein, 64% with beta-human chorionic gonadotropin, 53% with ultrasound and 67% with computerized tomography. Occasionally, alpha-fetoprotein or beta-human chorionic gonadotropin, or computerized tomography alone would be positive in a patient with stage B disease but ultrasound was never positive unless the computerized tomography scan also was positive. Based upon these results ultrasound scanning has been eliminated from the preoperative staging routine. Also, since the over-all accuracy in preoperatively evaluating patients with stages A and B nonseminomatous germ cell testis tumors is 70% retroperitoneal lymphadenectomy still is needed for accurate staging as well as for providing therapeutic benefit in the majority of patients with stage B disease. (Author abstract) (22 Refs)

49. SERUM FERRITIN AS A THIRD MARKER IN GERM CELL TUMORS.

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Eur J Cancer Clin Oncol; 18(3):261-269 1982

Serial measurements of serum ferritin have been assessed as an additional marker in a study of 12 patients with germ cell tumors. The standard markers, serum AFP and beta HCG, were also assessed serially. During treatment elevated levels of serum ferritin were detected in 10 patients, elevated AFP in 10 patients and elevated beta HCG in 6 patients. A poor prognosis was associated with persistently raised serum ferritin and either, or both, elevated AFP and beta HCG levels. Decreasing levels of serum ferritin indicated favorable response to treatment; rising values were associated with recurrence or dissemination of tumor. Even if serum ferritin cannot be classed specifically as a tumor product, it may be useful in the early detection of residual or recurrent tumor. (Author abstract) (20 Refs)

50. EVALUATION OF FOLLOW-UP METHODS TO DETECT RELAPSE AFTER MASTECTOMY IN BREAST CANCER PATIENTS.

Cantwell B, Fennelly JJ, Jones M
Dept. Medical Oncology, St. Vincent's Hosp., Elm Park, Dublin 4, Ireland
Ir J Med Sci; 151(1):1-5 1982

Out of 84 patients studied, 42 had recurrence of breast cancer, 1 patient developed a second primary carcinoma, and 41 patients remained disease free. The most useful means of first detection of recurrence was patient symptomatology: bone pain was most frequently reported and occurred in 24 (57.1%) who relapsed. Physical examination gave first evidence of relapse in 12 patients (28.5%). Frequent serial measurements were made of carcinoembryonic antigen, alkaline phosphatase and erythrocyte sedimentation rate; values were more commonly abnormal in patients with relapse. Although these tests are not entirely reliable, they are inexpensive, easy to perform, and may identify early distant metastases. Isotope bone scans and chest x-rays detected relapse reliably only in those patients with clinical abnormalities or abnormal blood tests. (16 Refs)

51. CARCINOEMBRYONIC ANTIGEN AS A MARKER IN PATIENTS WITH BREAST CANCER RECEIVING POSTSURGICAL ADJUVANT CHEMOTHERAPY.

Falkson HC, Falkson G, Portugal MA, Van Der Watt JJ, Schoeman HS
Dept. Cancer Chemotherapy, H. F. Verwoerd Hosp., Private Bag X169, Pretoria 0001, South Africa
Cancer; 49(9):1859-1865 1982

Serial plasma CEA levels were determined over a period of 1-3 yr in 114 patients receiving adjuvant chemotherapy for T1, 2 or 3a N+ MO breast cancer. CEA values were correlated with clinical status, scintiscans, and other biochemical parameters. CEA values greater than 2.5 ng/ml were considered abnormal. Forty-one patients had normal values throughout the adjuvant period. In 73 patients where abnormal values occurred, four different patterns were seen: (1) a statistically significant number (30/73) had initial elevations with a decreasing titer; (2) rising titer (10/73); (3) fluctuating titer of transient elevation (25/73); and (4) persistent elevation (8/73). Seventeen patients developed overt metastases, this was associated with a rising CEA in nine patients (p less than 0.002). CEA was more sensitive for predicting relapse than alkaline phosphatase of LDH. The correlation between CEA determination and the eventual development of metastatic disease is striking, and has implications for the design of future clinical trials. Results indicate that CEA could be used to identify high risk patients, to estimate efficacy of chemotherapeutic regime, and to determine optimal duration of therapy. (Author abstract) (9 Refs)

52. BIOCHEMICAL EVALUATION OF PATIENTS WITH BREAST CANCER.

Lee YT, Haymond HR, Feder B
Univ. Southern California Sch. Medicine, 1200 North State St., Los Angeles, CA, 90033
J Surg Oncol; 19(4):197-200 1982

Peripheral blood specimens were obtained from 50 patients with various stages of breast cancer (I-II = 7, III = 6, IV = 24, treated and NED = 13), and 20 biochemical tests were performed. There are significant differences of hemoglobin, LDH, SGPT, serum protein, albumin, and alpha globulin values between patients with early (I, II, NED) and late (III, IV) lesions. Among patients with Stage IV diseases, those patients with bony metastases had significantly higher values of alkaline phosphatase, alpha-1 globulin, IgA, and C-reactive protein than those with nonosseous lesions. Neither CEA nor pregnancy-associated alpha-2 glycoprotein showed any correlation with different stages or sites of breast cancer in these small series of patients. (Author abstract) (21 Refs)

53. CEA POSITIVITY IN TISSUE AND SERA OF PATIENTS WITH BENIGN BREAST LESIONS.

Wittekind C, Von Kleist S, Sandritter W
Institut fur Immunobiologie, Stefan-Meierstrasse 8, D 7800 Freiburg, W. Germany
Oncodev Biol Med; 2(6):381-390 1981

The presence of CEA was studied in paraffin sections of 100 benign breast lesions using an immunoperoxidase technique. In fibroadenomas, CEA was found in 25% of cases as opposed to 64% with cystic disease with or without epitheliosis. Our results demonstrate a tendency for an increased frequency of CEA tissue positivity in association with a more prominent form of epithelial hyperplasia with cystic disease. The observed higher positivity of tissue CEA may reflect a higher 'cellular activity' in the latter lesions compared with fibroadenomas. (Author abstract) (25 Refs)

54. DIAGNOSTIC VALUE OF CARCINOEMBRYONIC ANTIGEN ASSAY IN THE BLOOD SERA OF PATIENTS WITH CANCER OF THE LARYNX.

Lukach EV, Mel'nik LF
Dept. Oncological Otolaryngology, A. I. Kolomiichenko Res. Inst. Otolaryngology, Kiev, USSR
Zh Ushn Nos Gorl Bolezn; (1):13-16 1982

Diagnostic efficacy of carcinoembryonic antigen (CEA) determination was studied in 45 patients (31-70 yr old) with cancer of the larynx. Prior to the surgery, elevated concentrations of CEA were detected in 50% of the patients with Stage III-IV and in 80% of the patients with recurrent laryngeal cancer (43.7 and 120.5 nanog/ml, respectively, compared with 5.0 nanog/ml in healthy controls). Elevated concentrations of CEA were also observed in the patients with chronic laryngitis (16.9 nanog/ml). Successful surgery resulted in the decrease of CEA levels. These findings indicate that CEA assay can be used for the diagnosis of recurrence or metastases of laryngeal cancer. (17 Refs) (In RUS)

55. ADENOCARCINOMA OF THE PALATE ASSOCIATED WITH NEPHROTIC SYNDROME AND EPIMEMBRANOUS CARCINOEMBRYONIC ANTIGEN DEPOSITION.

Borochovitz D, Kam WK, Nolte M, Graner S, Kiss J
Dept. Pathology, Montefiore Hosp., 3459 Fifth Ave., Pittsburgh, PA, 15213
Cancer; 49(10):2097-2102 1982

A 42-yr-old male presented with adenocarcinoma of the palate and nephrotic syndrome. Renal biopsy demonstrated membranous glomerulopathy in which carcinoembryonic antigen was demonstrated. Carcinoembryonic antigen was also found in the palatal tumor. This is the first instance of this association with this particular tumor. (Author abstract) (29 Refs)

56. CARCINOEMBRYONIC ANTIGEN ASSAY IN THYROID SCREENING.

Shimaoka K, Chu TM
Dept. Clinical Pharmacology and Therapeutics, New York State Dept. Health, Roswell Park Memorial Inst., 666 Elm St., Buffalo, NY, 14263
J Cancer Res Clin Oncol; 103(1):99-103 1982

CEA assay was incorporated into a screening program in which a high risk population for thyroid diseases due to previous irradiation for benign conditions in the head and neck areas were studied. Seven hundred eleven CEA determinations were available from 735 patients screened; 22 (3.1%) were found to have an elevated level. This is compared to 31 (1.7%) from 1,875 healthy control subjects. Although the difference is statistically significant, we conclude the use of CEA assay in thyroid screening is not rewarding due to its lack of activity and specificity. (Author abstract) (8 Refs)

ULTRASTRUCTURE/ CYTOCHEMISTRY

57. AN IMMUNOHISTOCHEMICAL STUDY OF A SERIES OF PLASMA PROTEINS IN THE EARLY HUMAN CONCEPTUS.

Jacobsen GK, Jacobsen M, Henriksen OB
Dept. Pathological Anatomy, Herlev Hosp., DK-2730 Herlev, Denmark
Oncodev Biol Med; 2(6):399-410 1981

A 20-day-old human conceptus was studied by the indirect immunoperoxidase technique for the presence of a series of plasma proteins: prealbumin (PA), albumin (ALB), alpha-fetoprotein (AFP), alpha1-antitrypsin (A1 AT), carcinoembryonic antigen (CEA), immunoglobulin G (IgG), ferritin (FER), transferrin (TR), fetal hemoglobin (HbF), human chorionic gonadotropin (HCG), human placental lactogen (HPL) and pregnancy specific beta1-glycoprotein (SP1). In the embryo only FER and TR were found. The yolk sac was positively stained for several proteins: PA, ALB, AFP, A1 AT, IgG, FER, TR and HbF were demonstrated in the endodermal cells and PA, ALB, IgG and TR in the mesothelial cells. The syncytiotrophoblast of the chorionic villi were heavily stained for all the placental proteins. HCG and HPL were additionally demonstrated in the cytotrophoblast. The Hofbauer cells of the chorionic and villous stroma stained positively for A1 AT and FER. TR appeared as a characteristic band on the apical surface of the syncytiotrophoblast. The findings indicate that the yolk sac is the principal source of some of the plasma proteins also in the very early conceptus and the assumption that the yolk sac is the functional antecedent of the liver is supported. The distribution of the various placental proteins is in accordance with the present knowledge that the syncytiotrophoblast is the major site of synthesis of these proteins. Finally correlation of functional aspects of embryonic structures of germ cell tumors is recommended. (Author abstract) (24 Refs)

58. DETECTING CARCINOEMBRYONIC ANTIGEN (CEA) BY MEANS OF IMMUNOHISTOCHEMICAL METHODS.

Takagi J

Dept. Oral Pathology, Tokyo Medical and Dental Coll., Sch. Dentistry, Tokyo, Japan

Kokubyo Gakkai Zasshi; 48(4):479 1981

Immunohistochemical methods used to detect CEA by means of horseradish peroxidase, chemical properties of CEA, electron microscopic characteristics of CEA, research concerning detection of CEA in various types of cancers, and studies of CEA in oral cavity and parotid gland tumors were discussed. Some studies indicated that CEA is not detectable in squamous cell carcinomas originating in the oral mucosa or in soft tissue tumors. Other studies indicated that high levels of CEA are detectable in normal and cancerous parotid gland tumors. The significance of the high levels of CEA in normal and cancerous parotid glands was thought to be a current topic of debate. (2 Refs) (In JPN)

59. IMMUNOLOGIC-HISTOCHEMICAL DETECTION OF BETA-HCG IN A SEMINOMATOUS TESTICULAR TUMOR.

Carbone A, Caillaud JM

Istituto scientifico per lo studio e la cura di tumori, Universita di Genova, Genova, Italy

Pathologica; 73(1027):805-810 1981

A 32-yr-old man with a prior left orchiectomy noted a tumor which appeared 4 mo previously. Serum beta-human chorionic gonadotropin (HCG) was negative. Histologic diagnosis was seminoma stage T1N0M0. The patient was administered radiotherapy (4,000 rad). After 2 yr, serum was negative for beta-HCG and alpha-fetoprotein (AFT). Reexamination of the histologic material showed infiltration of malignant tissue, rare mitoses, and rare giant cells with intensely colored multiple nuclei indicating seminoma. The indirect immunoperoxidase test using peroxidase-anti-peroxidase (PAP) test produced positive results. Differentiation of seminoma from pseudo-seminoma should be performed by determination of the beta-HCG and AFT in serum before surgery, histologic examination and the PAP test of the tissue removed. (22 Refs) (In ITA)

60. IMMUNOHISTOCHEMICAL EVALUATION OF CARCINOEMBRYONIC ANTIGEN, SECRETORY COMPONENT, AND EPITHELIAL IGA IN ULCERATIVE COLITIS WITH DYSPLASIA.

Rognum TO, Elgjo K, Fausa O, Brandtzaeg P

Histochemical Lab., Inst. Pathology, Rikshospitalet, Oslo 1, Norway

Gut; 23(2):123-133 1982

Immunofluorescence staining for carcinoembryonic antigen, secretory component, and epithelial IgA was evaluated semiquantitatively in routine formalin-fixed mucosal biopsy samples from five patients with ulcerative colitis who had undergone colectomy because of carcinomas. The two types of lesion did not differ significantly with regard to the expression of the three marker antigens. In a prospective study based on cold ethanol-fixed mucosal biopsy samples, lesions from 11 ulcerative colitis patients with dysplasia were compared blindly with lesions from 6 patients with reactive hyperplasia and with samples obtained endoscopically from 8 normal controls. The range of disease-associated fluorescence intensity scores was wide. The wide ranges of individual fluorescence scores precluded the possibility of applying carcinoembryonic antigen, secretory component, and epithelial IgA as immunohistochemical markers to differentiate between dysplasia and reactive hyperplasia in routine diagnostic work. (43 Refs)

61. ULTRASTRUCTURAL LOCALIZATION OF CARCINOEMBRYONIC ANTIGEN IN NORMAL INTESTINE AND COLON CANCER. ABNORMAL DISTRIBUTION OF CEA ON THE SURFACES OF COLON CANCER CELLS.

Ahnen DJ, Nakane PK, Brown WR

(c/o Brown), Veterans Admin. Medical Center, 111E, 1055 Clermont St., Denver, CO, 80220

Cancer; 49(10):2077-2090 1982

The distribution of carcinoembryonic antigen (CEA) in normal small intestine, normal colon, and colon cancer of humans was determined immunocytochemically by the peroxidase-labeled antibody method at the light and electron microscopic levels. In the small intestine, CEA was found in protein synthetic organelles, in the mucus, on the microvilli of goblet cells, and on some microvilli of columnar cells adjacent to goblet cells. In the normal colon, CEA was found in protein synthetic organelles of the fully differentiated columnar cells and goblet cells, as well as on the microvilli of the cells. In two well-differentiated colon cancers, the normal preferential surface expression of CEA on the microvilli was maintained, but in six poorly differentiated cancers, CEA was distributed equally over the entire cell surface. We conclude that CEA is a product of goblet cells in the small intestine, columnar and goblet cells in the colon, and colonic cancer cells. CEA on the surfaces of the normal epithelial cells is expressed in a polar manner. This polarity is lacking in undifferentiated neoplastic colon cells, which suggests that failure to establish or maintain the polar expression of normal cell-surface glycoproteins is a characteristic of the neoplastic cells. (Author abstract) (51 Refs)

62. CARCINOEMBRYONIC ANTIGEN IN BENIGN SWEAT GLAND TUMORS.

Penneys NS, Nadji M, Morales A
Dept. Dermatology, Univ. Miami Sch. Medicine, P.O. Box 016940, Miami, FL, 33101
Arch Dermatol; 118(4):225-227 1982

Carcinoembryonic antigen was demonstrated in sweat gland adenomas by immunostaining using standard immunoperoxidase techniques. Carcinoembryonic antigen could not be found in adnexal tumors derived from the pilar and sebaceous apparatus. The demonstration of this specific antigen in certain sweat gland tumors may be helpful in the recognition and classification of these kinds of lesions. (Author abstract) (12 Refs)

63. PALE EOSINOPHILIC INCLUSIONS SIMULATING GROUND-GLASS APPEARANCE OF CELLS OF HEPATOCELLULAR CARCINOMA.

Nakanuma Y, Kono N, Ohta G, Shirasaki S, Takeshita H, Watanabe K, Tsuda S, Yoshizawa H
Second Dept. Pathology Sch. Medicine, Kanazawa Univ., Takaramachi 13-1, Kanazawa 920, Japan
Acta Pathol Jpn; 32(1):71-81 1982

Pale eosinophilic inclusions simulating ground-glass appearance were observed in cells of hepatocellular carcinoma. They were round or elliptical in shape, and their size was about 14 um in diameter. Light eosinophilia and fine granulation with homogeneous appearance were delineated from other cellular materials. They were negative for HBsAg, blood plasma proteins including alpha1-antitrypsin, and alpha-fetoprotein by immunohistochemical stainings. Ultrastructurally, they were well-demarcated and consisted of homogeneous finely granular matrix. Histological, histochemical and ultrastructural features were different from several intracellular inclusions hitherto reported on hepatocellular carcinoma. These changes may represent a deposition of secretory proteinous materials in cells of hepatocellular carcinoma, but their chemical and antigenetical content could not be identified. (Author abstract) (25 Refs)

64. POLYEMBRYOMA OF OVARY PRODUCING ALPHA-FETOPROTEIN AND HCG: IMMUNOPEROXIDASE AND ELECTRON MICROSCOPIC STUDY.

Takeda A, Ishizuka T, Goto T, Goto S, Ohta M, Tomoda Y, Hoshino M
Lab. Ultrastructure Res., Aichi Cancer Center Res. Inst., Chikusaku, Nagoya 464, Japan
Cancer; 49(9):1878-1889 1982

Polyembryoma of ovary producing alpha-fetoprotein (AFP) and human chorionic gonadotropin (HCG) was studied by indirect immunoperoxidase method for AFP and HCG, and electron microscopy. Clinically, this patient showed pseudoprecocious puberty caused by elevated HCG which is synthesized by trophoblastic cells in polyembryoma. She is put under VAC (vincristine, actinomycin-D, cyclophosphamide) chemotherapy after operation and shows no signs of recurrence including reelevation of serum AFP at 5 mo after operation. Embryoid bodies which we studied correspond to normal embryo at 15- or 16-day stage. Immunoperoxidase study showed that AFP is synthesized by yolk sac cells of the embryoid bodies and HCG is synthesized by syncytiotrophoblastic cells. The finding about AFP synthesis suggests that normal embryo at 15-or 16-day stage may begin AFP synthesis. Electron microscopic study showed that each part of the embryoid bodies had some characteristic structures. Most striking features found in the cytodifferentiation of the embryoid bodies were noticed in some special differentiation of plasma membrane and existence of surface coat. Desmosomes were found in endodermal cells and yolk sac cells. Ectodermal cells were attached to each other by zonulae occludentes and adherentes. Microvilli were found in ectodermal cells and yolk sac cells. Two different kinds of surface coat were found in mesodermal cells and lining cells of yolk sac cavity: thin-layered deposit of electron-dense material covering the plasma membrane facing intercellular space of mesodermal cells and endodermal cells, and thick-layered deposit of electron-dense material which covered the plasma membrane facing yolk sac cavity of endodermal cells and yolk sac cells. Presence of similar characteristic material in RER of yolk sac cells led us to speculate that thick deposit was synthesized by yolk sac cells and secreted into yolk sac cavity. Combined with immunoperoxidase study by light microscopy, we assume that this thick-layered deposit has some close relation to AFP. (Author abstract) (23 Refs)

65. CHARACTERIZATION OF ALPHA-TISSUE ANTIGEN (ALPHATA), A MEMBRANE GLYCOPROTEIN OF CANCER CELLS.

Yachi A, Kawaharada M, Akahonai Y, Imai K, Wada T
Dept. Internal Medicine (Section 1), Sapporo Medical Coll., Sapporo, Japan
Protides Biol Fluid Proc Colloq; 29:93-96 1982

An immunochemical, biochemical and immunohistological study is presented of alpha-tissue antigen (aAT) isolated from perchloric acid soluble extracts of cancer tissue. The aAT is a glycoprotein with a mol wt of 41,000 daltons, an isoelectric pH of 3.4, and a sugar content of 10%. It is antigenically distinct from membrane associated tissular autoantigen of van Kleist as well as from other tumor associated antigens including carcinoembryonic antigen, alpha-fetoprotein and ferritin. While not cancer specific, immunofluorescent and rosette formation studies indicate aAT may be membrane-associated on cancer cells. (4 Refs)

REVIEWS/ OTHER RELATED STUDIES

66. COLORECTAL CANCER.

Sugarbaker PH, MacDonald JS, Gunderson LL
NCI, NIH, Bethesda, MD
Cancer - Principles and Practice of Oncology. DeVita VT, Hellman S, and Rosenberg SA, ed. Philadelphia, Lippincott, 1926 pp., 1982.

The anatomy of the large bowel, and the pathobiology and treatment of neoplastic lesions of the large bowel are described and illustrated in detail. Gross anatomy of the colon, histology and physiology of colonic epithelium, epidemiology of colonic neoplasms, natural history of surgically treated colorectal cancer, patterns of recurrence, pathology (including growth patterns of normal and abnormal mucosa), staging of colonic cancer, prognosis, clinical features and their effect on prognosis (including diagnosis in asymptomatic patients, long duration of symptoms, preoperative carcinoembryonic antigen determination), pathological features and their effect on prognosis, screening for cancer in asymptomatic patient populations, screening techniques for colorectal cancer, diagnosis of colorectal cancer in the symptomatic patient, constricting lesions from large bowel cancer, diagnosis of recurrent colorectal cancer, treatment of colorectal polyps, principles of surgical treatment of colorectal cancer, principles of radiation therapy of colorectal cancer, principles of chemotherapy for colorectal cancer, treatment of primary colorectal cancer, treatment of rectal cancer, adjuvant chemotherapy, and treatment of recurrent and disseminated disease are discussed. (578 Refs)

67. ANTIGENICITIES OF MUCINS - THEIR RELEVANCE TO TUMOUR ASSOCIATED AND STAGE SPECIFIC EMBRYONIC ANTIGENS.

Feizi T
Applied Immunochemistry Res. Group, Div. Communicable Diseases, Clinical Res. Centre, Harrow, Middlesex, England
Adv Exp Med Biol; 144:29-37 1982

Differentiation antigens expressed in secreted glycoproteins are reviewed. Secreted glycoproteins have provided fundamental information on the nature of the major blood group antigens and their precursors. Blood group branched (I) and linear antigens are expressed on type 2 precursor chains; the expression of I antigen of 'Ma type' in gastric mucins is genetically determined. Changes in antigenicity of gastric mucosal glycoproteins associated with cancer are discussed. Mucins could serve as valuable sources of oligosaccharide haptens of differentiation antigens. (17 Refs)

68. REGULATION OF THE CELLULAR P53 TUMOR ANTIGEN IN TERATOCARCINOMA CELLS AND THEIR DIFFERENTIATED PROGENY.

Oren M, Reich NC, Levine AJ
Dept. Microbiology, Sch. Medicine, State Univ. New York at Stony Brook, Stony Brook, NY, 11794
Mol Cell Biol; 2(4):443-449 1982

The regulation of a 53,000-mol wt cellular tumor antigen, p53, in F9 embryonal carcinoma cells was investigated. Treatment of F9 cells with retinoic acid and dibutyryl ADP causes the cells to differentiate, predominantly into endoderm-like cells, and results in a marked decrease in the levels of p53. The mechanism(s) responsible for the decline in p53 in differentiated cells involves a marked decrease in the amount of in vitro translatable p53 messenger RNA. This mechanism is discussed with respect to that operating in simian virus 40 infection or transformation and which involves increased stability of the p53 protein. (22 Refs)

69. TESTICULAR TUMOR MARKERS.

Scardino PT
Dept. Urology, Baylor Coll. Medicine, Houston, TX
Cancer Bull; 34(1):9-16 1982

Historical background, frequency of elevated markers, source of markers, and value of the markers in care of patients with testicular tumors are reviewed. Current practice in treatment of testicular tumors includes determinations of the presence and quantity of human chorionic gonadotropin (hCG) and alpha-fetoprotein (aFP), which closely reflect the nature, extent, and activity of these tumors in the patients. The frequency of elevated markers in nonseminomas reflects the extent, or pathologic stage, of the tumor, but in seminomas the meaning of elevated levels is controversial. Serum marker levels are valuable in diagnosis, staging, and long-term monitoring, but prognostic value is uncertain. Other biochemical markers of testicular cancer have been identified, but none adds sufficient information to that from hCG to warrant use in routine assay. Lactate dehydrogenase is an inexpensive, useful nonspecific tumor marker. The use of hCG and aFP markers has increased the accuracy of diagnosis and staging, revolutionized understanding of tumor histology, and substantially improved monitoring ability. The value of serial measurements of both hCG and aFP before and after each phase of treatment of testicular tumor is emphasized. (26 Refs)

70. MULTIPLE CELL LINES FROM PATIENTS WITH MALIGNANT MELANOMA: MORPHOLOGY, KARYOLOGY, AND BIOCHEMICAL ANALYSIS.

Semple TU, Moore GE, Morgan RT, Woods LK, Quinn LA
Div. Surgical Oncology, Denver General Hosp., 750 Cherokee St., Denver, CO, 80204
JNCI; 68(3):365-380 1982

Of 23 cell lines representing eight patients with malignant melanoma, one cell line from each patient has been extensively characterized by means of phase morphology, ultrastructural morphology, biochemical markers, steroid receptor protein analysis, and steroid hormone production. Extensive cytogenetic characterization was compiled from seven of the eight cell lines. The melanocytic derivation of the tumor cell lines was supported by the detection of the catecholamines epinephrine, norepinephrine, and dopamine. In addition, well-defined melanosomes were present in six of the seven lines whose ultrastructures were examined morphologically. None of the lines produced alpha-fetoprotein, beta-human chorionic gonadotropin, or carcinoembryonic antigen in detectable amounts. The individuality of the cell lines was confirmed by phenotypic patterns of isozymes and by karyology. (Author abstract) (16 Refs)

71. ABSENCE OF MELANOMA SPECIFICITY IN THE REACTIVITY OF MELANOMA PATIENTS' SERA WITH CULTURED ALLOGENEIC MELANOMA CELL LINES.

Dent PB, Liao SK, McCulloch PB, Stone BR, Singal DP
Dept. Pediatrics, Ontario Cancer Treatment and Res. Foundation, Hamilton Clinic, Hamilton, Ontario, L8N 3Z5, Canada
Cancer; 49(10):2043-2048 1982

While patients with melanoma are known to produce antibodies against melanoma cells, the tumor specificity of these reactions has not been well documented. Using the sensitive mixed hemadsorption assay we have identified antibody against one or more of nine different cultured melanoma cell lines in only 9 of 48 patients with melanoma. Reactivity against melanoma cell lines was seen only in females, 9/27 vs 0/21 males. The strongest melanoma reactivity was seen in sera which also contained lymphocytotoxic antibody. The reactivity was not melanoma specific because it could be removed by absorption either with pooled platelets, nonmelanoma tumor cells or in two cases, by both. We conclude that the occurrence of specific antimelanoma antibodies against common or shared surface melanoma associated antigens is an uncommon event in melanoma patients not receiving specific active immunotherapy. The clinical significance of the observed reactivity and whether it is directed against cancer associated determinants, fetal antigens, or normal tissue or histocompatibility antigens requires further study. (Author abstract) (31 Refs)

72. DRUG TARGETING WITH MONOCLONAL ANTIBODIES.

Page M, Emond JP, Gauthier C, Dufour C, Innes L
Dept. Biochemistry, Universite Laval, Quebec, Canada
Protides Biol Fluid Proc Colloq; 29:933-936 1982

Conjugates of daunomycin (DAU) with anti-carcinoembryonic antigen (CEA) were prepared by covalently binding DAU to monoclonal antibodies with 0.01% glutaraldehyde. The pharmacological activity of the conjugate was assayed in vitro with human colon adenocarcinoma cells producing CEA (Lovo cells). At a drug:protein ratio of 5.7, the inhibition of thymidine incorporation was measured at various concentrations. At 500 nanog/ml, the DAU monoclonal anti-CEA conjugate was 8x more active than free DAU. The total inhibition of thymidine incorporation was only slightly better than that for free DAU when DAU plus monoclonal antibody were used. Free monoclonal anti-CEA did not affect thymidine incorporation. Compared with 0.1, 0.2, and 0.5 ug/ml of free DAU, inhibition of thymidine incorporation by the conjugate was increased by at least 2x. These results demonstrate that monoclonal conjugates retain both their pharmacological and immunological activity and that monoclonal anti-CEA can be a drug carrier for cancer treatment. (8 Refs)

73. THE POTENTIAL USE OF MONOCLONAL ANTIBODIES IN DRUG TARGETING.

Rowland GF, Simmonds RG, Corvalan JR, Marsden CH, Johnson JR, Woodhouse CS, Ford CH, Newman CE
Lilly Res. Centre, Erl Wood Manor, Windlesham, Surrey, England
Protides Biol Fluid Proc Colloq; 29:921-926 1982

Conjugates of vindesine (VDS) and polyclonal antibodies were prepared. In vitro targeting was demonstrated with an indirect or 'sandwich' technique. VDS-goat anti-rabbit conjugates were used with either mouse T lymphoma cells (EL4) or human anaplastic lung tumor cells (CALU-6). Cells were exposed to appropriate rabbit antiserum for 30 min, unbound antibody was washed away, and the cells were further incubated with VDS-goat anti-rabbit antibody. The number of EL4 cells increased during the first 24 hr of growth following such treatment. Similar results were obtained with CALU-6 cells following 2 hr of incubation. Cytostatic effects were obtained in both cell types only when the VDS conjugate could recognize the first layer antibody as a target. When VDS-sheep anti-carcinoembryonic antigen (CEA) IgG was used, the VDS-antibody conjugate was more cytotoxic than free VDS, mixtures of VDS and antibody, or a conjugate of VDS and normal sheep IgG. Approx 25x less conjugated VDS was necessary than free VDS to kill 50% of the cells. Several fusions were attempted in order to produce specific monoclonal anti-CEA antibodies; a high yield of active hybridomas was achieved. (10 Refs)

74. APPLICATION OF HUMAN EMBRYONIC ANTIGEN FOR IDENTIFICATION OF IMMUNE RESPONSE IN CANCER PATIENTS.

Gorodilova VV, Mandrik EV, Ul'chenko VM
P. A. Herzen Res. Inst. Oncology, RSFSR Ministry Health, Moscow, USSR
Vopr Onkol; 28(1):23-27 1982

The study was concerned with a comparison of immune response to antigen obtained from human embryonic intestine in patients with malignant and benign tumors of the breast and ovaries, cancer of the urinary bladder, cases of various inflammatory diseases and healthy controls. Application of this marker in the skin test of time-delayed hypersensitivity reaction provided a means of evaluation of tumor-associated immunological vigor. The results point to the similarity of skin reactions of time-delayed hypersensitivity in cases of mastopathy and early stages of breast cancer. Therefore, human embryonic antigen may be used as an additional criterion of assessment of immunocompetence of patients with precancerous lesions and malignant neoplasms. (Author abstract) (10 Refs) (In RUS)

75. SWEDISH-NORWEGIAN NONSEMINOMATOUS TESTICULAR TUMOR DIAGNOSIS AND THE THERAPY PROJECT (SWENOTECA).

Fossa SD, Dahl O, Due J, Grottum KA, Hoisaether PA, Klepp O, Mjolnerud O, Ous S, Sander S, Tveter K, Uriaastad M
Alminnelig avdeling, Det Norske Radiumhospital, Montebello, Oslo 3, Norway
Tidsskr Nor Laegeforen; 102(6):371-374 1982

A joint Swedish-Norwegian protocol for the diagnosis, therapy and follow-up of nonseminomatous testicular tumors is presented. Diagnosis and staging includes thorough clinical examination, chest x-ray complemented by frontal planigraphy, bilateral lymphography to detect retroperitoneal lymph node metastases, abdominal and pelvic computer tomography and/or ultrasonography, urography, and repeated determinations of the serum levels of alpha-fetoprotein and human chorionic gonadotropin. Inguinal orchiectomy is the first step in primary treatment. Irradiation will be replaced by routine retroperitoneal lymphadenectomy as part of primary treatment in Stages I, IIA and partly in IIB. Intensive cytostatic therapy will be instituted in more advanced stages to render the patients operable or to destroy disseminated micrometastases. Chemotherapy must be followed by radical lymphadenectomy, if chemotherapy was not completely successful. The tumor-free 3-yr survival rates after the start of the treatment can be expected to be 90-100% in Stage I, 85-95% in Stages IIA and IIB, 70-85% in IIC, and 30-50% in III-IV. Thorough and frequent follow-up is required during the first 2 yr after the completion of therapy. (13 Refs) (In NOR)

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ONCOFETAL PROTEINS

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STRUCTURE/ IDENTIFICATION/ CHARACTERIZATION

1. A MONOCLONAL ANTIBODY (B72.3) DEFINES PATTERNS OF DISTRIBUTION OF A NOVEL TUMOR-ASSOCIATED ANTIGEN IN HUMAN MAMMARY CARCINOMA CELL POPULATIONS.

Nuti M, Teramoto YA, Mariani-Costantini R, Hand PH, Colcher D, Schlom J
Lab. Cellular and Molecular Biology, NCI, NIH, Bethesda, MD, 20205
Int J Cancer; 29(5):539-545 1982

We report here both the range and patterns of reactivity of an IgG1 monoclonal antibody, B72.3, prepared against human metastatic mammary carcinoma cells. When the avidin-biotin complex (ABC) immunoperoxidase technique was used on tissue sections, monoclonal B72.3 reacted with 19 of 41 (46%) primary mammary carcinomas and 13 of 21 (62%) metastatic lesions, either in axillary lymph nodes or at distal sites. Variable concentrations of antigen, recognized by B72.3, were observed among mammary tumors, as well as among different cell populations of a given tumor mass. Several patterns of

HE 20.3173/2:

antigen distribution were observed: membrane, diffuse cytoplasmic, focal, apical and marginal. No reactivity was observed to normal mammary epithelium, stroma, or lymphocytes of the breast, nor to any cell types in a variety of other normal human tissues, melanomas, and sarcomas. Reactivity with all of four colon carcinomas was also observed. Assay of serial sections of mammary carcinomas with B72.3 and a monoclonal antibody directed against carcinoembryonic antigen demonstrated that these antigens were both distinct and non-coordinately expressed. (Author abstract) (17 Refs)

2. A COMMON MEMBRANE ANTIGEN IN HUMAN TUMOR SPECIMENS DETECTED WITH MONOCLONAL ANTIBODIES (MEETING ABSTRACT)

Brown JM
Division of Surgical Oncology, University of Illinois, P.O. Box 6998, Chicago, IL, 60680
Proc Am Assoc Cancer Res; 23:1042 1982

Hybridoma technology was utilized to produce monoclonal antibodies reactive with tumor-associated membrane antigens of human tissue specimens. Membrane fractions enriched in plasma membranes by gradient centrifugation were prepared from tumor and normal tissues. Spleen cells from a BALB/c mouse immunized with tumor membranes of a patient with malignant fibrous histiocytoma (MFH) were fused with mouse myeloma X63-Ag8.653 by standard techniques. Supernatants of the resultant hybridoma clones were initially screened for antibody binding to the immunizing MFH membranes but not to membranes from a normal allogeneic spleen. Subsequent culture and testing for binding to a large panel of membranes identified two monoclonal antibodies, 19-14 and 19-24, reactive with tumor but not with normal adult tissues. The antibodies, both of isotype IgG1, demonstrated identical patterns of reactivity. Significant binding was observed with membranes from 4/4 MFH tumors tested, 7/8 osteosarcomas, 1/1 melanoma, 1/1 pooled first trimester human fetal specimen, 0/5 skeletal muscle specimens, 0/2 spleens, 0/1 lymph node, and 0/1 erythrocyte specimen from the immunizing MFH patient. Antibody reactivities were specifically removed by absorption with MFH and osteosarcoma membranes, but not with muscle membranes. The results suggest that a common membrane antigen, possibly oncofetal, has been detected in tumors of several different histologies including MFH, osteosarcoma, and melanoma, in tissues of the first trimester fetus, but not in a number of normal adult tissues. (no Refs)

3. HUMAN TUMOR NUCLEOLAR ANTIGENS: MONOCLONAL ANTIBODIES, 2D GEL ANALYSIS AND PCNA (MEETING ABSTRACT)

Son M, Kelsey DE, Chan PK, Frakes RB, O'Leary PJ, Spohn WH, Tan E, Busch RK, Busch H
Department of Pharmacology, Baylor College of Medicine, Houston, TX, 77030
Proc Am Assoc Cancer Res; 23:1073 1982

The evidence for the presence of common nucleolar antigens in a broad range of carcinomas, sarcomas and hematological malignancies led to present attempts to purify individual tumor nucleolar antigens. One antigen (54/6.3) was purified from the 100,000 g supernatant of the 0.01 M Tris-HCl extract by ammonium sulfate fractionation, DEAE (diethylaminoethyl) chromatography and affinity chromatography. Additional antigens with MW 96, 90, 80, 68 and 61 kdaltons were purified from HeLa and Namalwa RNP fractions and identified by 1 and 2D gel 'Western blots'. Monoclonal antibodies to nucleolar antigens were obtained from hybridomas; the mouse myeloma P3 x 63 Ag 8.653, a nonsecretor, was used for fusions. The spleen cells were taken from mice immunized with 0.25 M NaCl eluate from DE 52 cellulose of a 0.01 M Tris Namalwa nuclear extract. Several hybridomas had higher ELISA activity with the HeLa and Namalwa Tris and RNP extracts than with the normal liver fractions. As yet, none has the same specificity for malignant tumors as found previously with the rabbit antitumor nucleolar antibodies. PCNA (proliferating cell nuclear antigen) antibodies from a patient with lupus erythematosus had nucleolar localization in several tumors instead of general nuclear localization in nontumor tissues. Nucleolar antigens of human tumors appear to be a complex of oncofetal antigens, such as PCNA which is transported into the nucleolus in the G1/S phase. (4 Refs)

4. MONOCLONAL ANTIBODIES DIRECTED AGAINST THE SUGAR SEQUENCE OF LACTO-N-FUCOPENTAOSE III OBTAINED FROM MICE IMMUNIZED WITH HUMAN TUMORS (MEETING ABSTRACT)

Brockhaus M, Magnani J, Herlyn M, Blaszczyk M, Ginsburg V
National Institutes of Health, Bethesda, MD, 20205
Fed Proc; 41(3):897 1982

Four hybridomas obtained from mice immunized with human colon or stomach adenocarcinomas produce antibodies that bind to glycolipids of erythrocytes, granulocytes and various normal and malignant tissues. Binding of the antibodies to the glycolipids is inhibited by lacto-N-fucopentaose III, but not by the structurally related oligosaccharides lacto-N-tetraose, lacto-N-fucopentaose I and lacto-N-difucohexaose I. The antibodies bind specifically in solid-phase radioimmunoassay to the ceramide pentasaccharide that contains the lacto-N-fucopentaose III sequence of sugars. Thus, these antibodies have the same specificity as reported for a monoclonal antibody against a stage-specific antigen of the murine embryo. (2 Refs)

5. MELANOMA AND GASTROINTESTINAL ADENOCARCINOMA ONCOFETAL ANTIGENS DEFINED BY MONOCLONAL ANTIBODIES (MEETING ABSTRACT)

Steplewski Z, Herlyn M, Mitchell K, Herlyn D, Blaszczyk M, Koprowski H
The Wistar Institute, Philadelphia, PA, 19104
Hybridoma; 1(2):183 1982

Five groups of antigens were detected on the surface of human melanoma cells by a panel of 35 different monoclonal antibodies. In Group I, antigens were expressed only by melanoma cells. Group II antigens, detected by six monoclonal antibodies, are high molecular weight (MW) glycoproteins (260K and 290K). These antigens are expressed not only by melanoma cells, but also by other tumor cells of neural tube origin and by pigmented embryonal cells and represent the oncofetal protein group. Anti-melanoma monoclonal antibodies against group III antigens also bind to some lung carcinomas and one sarcoma, but do not bind to tumors of neural tube origin. Six anti-melanoma antibodies of Group IV bind to antigens with MW 85K and 120K and are also expressed on other tumors and on embryonal pigmented cells, but not on normal adult cells. In Group V, melanoma-associated antigens include DR-antigen and a group of antigens with different molecular sizes (79K, 119K and 139K) which are expressed on a variety of tumor cells, some embryonal cells, and some specialized normal cells. In gastrointestinal adenocarcinomas, monoclonal antibody-defined glycolipid antigens include a ganglioside containing sialylated lacto-N-fucopentaose II. This antigen is expressed in tumor cells and is detected in serum of patients with adenocarcinomas of stomach, pancreas and colon. The same antigen is present in meconium; thus, it is also an oncofetal antigen. Other anti-glycolipid monoclonal antibodies detect blood group B antigens, Lewisb antigen and a lacto-N-fucopentaose III. (no Refs)

6. CONSECUTIVE ISOLATION OF SEVERAL COLONIC ANTIGENS (MEETING ABSTRACT)

Gold DV, Shochat D, Pant KD, Bennett SJ, Goldenberg DM
University of Kentucky Medical Center, Lexington, KY, 40536
Fed Proc; 41(3):554 1982

Human colon mucosa and its tumors produce several antigens, among them colon specific antigen-p (CSAp), colon specific antigen (CSA), colonic mucoprotein antigen (CMA) and carcinoembryonic antigen (CEA). CEA and CSAp have been shown to be useful in the detection and monitoring of colon cancer and in radioimmunodetection. The clinical potential of the other two antigens is under investigation. Here we propose a comparatively simple procedure for the consecutive isolation of these antigens from a single tissue preparation. Gel filtration chromatography on Sepharose CL-4B was used as the first step in purification. CSAp, CSA, CMA and a large portion of the CEA co-eluted with the void volume fraction. The CEA was isolated from the CSAp, and both of these from the CMA and the CSA by chromatography on hydroxylapatite employing either step or linear phosphate gradients containing 0.1% sodium dodecyl sulfate. Both the CSA and the CMA did not bind to the gel 0.01M phosphate. The CEA was eluted between 0.1 and 0.17M phosphate, and the CSAp with phosphate concentrations around 0.32M. The recoveries of CSAp and CEA were 65% and 45% respectively. Immunodiffusion analysis revealed that CSA and CMA were immunologically related. (no Refs)

7. INITIAL CHARACTERIZATION OF A NEW TUMOR-ASSOCIATED ANTIGEN (MEETING ABSTRACT)

Brown C, Huang J, Rock HS
Lancer, Division of Sherwood Medical, Foster City, CA, 94404
Fed Proc; 41(3):885 1982

A new tumor-associated antigen (TAG) can be isolated by perchloric acid extraction of carcinomas of the gastrointestinal tract. The present isolation procedure involves passage of the dialyzed perchloric acid extract through an affinity column containing rabbit anti-TAG bound to Sepharose 4B. After elution of the bound material from this column, further affinity chromatography is carried out using Sepharose-bound antibodies to proteins commonly found as contaminants in such perchloric acid extracts. Analysis by SDS-PAGE (sodium dodecyl sulfate-polyacrylamide gel electrophoresis) indicates a molecular weight of 50,000-60,000 daltons. Examination of sliced-gel eluates obtained from SDS-PAGE electrophoresis of CEA and TAG indicates no overlap of staining of the two proteins and no measurable CEA (carcinoembryonic antigen) activity in the area of the gel where TAG was found. The isoelectric point has been found to be 4.5. Silver staining of the IEF (isoelectric focusing) gel indicates only one major band. Amino acid analysis of TAG indicates that it is rich in aspartic and glutamic acids, or the corresponding amides; leucine is also a major amino acid. With respect to sulfur amino acids, no cysteine is found, but methionine is present. N-terminal sequence analysis indicates a pattern which differs from other characterized glycoproteins known to be associated with carcinoma. Sugars constitute approximately 30% of the total mass of TAG. The exact nature of the sugar constituents is presently under investigation. (no Refs)

8. IMMUNOLOGIC ANALYSIS OF GLYCOPROTEINS RELEASED TO CULTURE MEDIUM IN VITRO BY HUMAN OVARIAN CARCINOMA CELLS (MEETING ABSTRACT)

Johnson EA, Piver MS, Gamarra M, Allen HJ
Roswell Park Memorial Institute, Buffalo, NY, 14263
Proc Am Assoc Cancer Res; 23:994 1982

We have begun an immunologic analysis of glycoproteins released by human ovarian carcinoma cells. Mucinous (Mu), Serous (Se), serous-endometroid (S-E) and clear cell (CC) adenocarcinoma cell clusters were isolated from effusions and incubated without protein supplement to generate antigen(s). The following antisera gave no reaction with culture medium components by immunodiffusion: anti-haptoglobulin, -alpha2-macroglobulin, -beta2-microglobulin, -fibrinogen, alpha-lipoprotein, -beta-lipoprotein, -fibronectin, -secretory component, -IgA, -IgM and -alpha1-acid glycoprotein. Anti-whole serum reacted with culture medium from Mu, S-E, CC and Se adenocarcinoma cells. Rabbit anti-globulin, - [IgG+IgA+IgM] and -IgG reacted with S-E and CC as did goat anti-[IgG+IgA+IgM]. Mu, S-E, Se and CC showed reaction of identity when tested against anti-Mu, -S-E, -Se, and -normal ovary (NO). Anti-Mu, -S-E, -Se, and -NO showed a reaction of identity with each culture medium. Immunoprecipitation experiments with metabolically labeled culture medium and iodinated (125I) pooled NO extract also demonstrated antigenic cross-reactivity. Commercial goat anti-CEA precipitated labeled glycoproteins whereas colon carcinoma-specific rabbit anti-CEA did not. These data indicate that ovarian carcinoma cells of different histologic types release a common antigen in vitro which is also present in normal ovary. The CEA released appears related to but not identical with colon CEA. The reactivity with anti-immunoglobulin (Ig) could be due to specific adsorption in vivo and release of Ig in vitro. (no Refs)

ASSAY PROCEDURES/ SYNTHESIS

9. ENZYME IMMUNOASSAY OF HUMAN ALPHA(1)-FETOPROTEIN.

Belanger L, Masseyeff R
Molecular Oncology Lab., L'Hotel-Dieu de Quebec Res. Center, Laval Univ., Quebec G1R 2J6, Canada
Methods Enzymol; 84:19-31 1982

Double antibody enzyme immunoassay and sandwich enzyme immunoassay of human alpha1-fetoprotein are discussed. The double antibody assay is a competitive system adapted from conventional radioimmunoassays that adhere to general principles of saturation analysis. Enzyme-labeled and unlabeled antigens compete for a limited amount of antibody and the extent of tracer-antibody reaction measures the amount of unlabeled antigen reacting in the system. The sandwich assay is a noncompetitive system adapted from two-site immunoradiometric assays. (16 Refs)

10. QUANTITATIVE AND QUALITATIVE DIFFERENCES IN 125I CEA LABELLED AT DIFFERENT CONCENTRATIONS.

Bartorelli A, Biancardi C, Ferrara R, Cavalca V, Ballo M, Accinni R
Istituto di Ricerche Cardiovascolari, c/o Centro Cardiologico, Via Bonfadini, 214-20138 Milano, Italy
Boll Ist Sieroter Milan; 60(6):489-493 1981

Qualitative and quantitative differences are described in three preparations of carcinoembryonic antigen (CEA) labeled with Na 125I at concentrations equivalent to or less than 0.5 mg/ml. Dilutions used contained per 10 ul, 5.0 to 0.00625 ug of labeled CEA, with specific activities ranging from 54 to 7.3 uCi/ug. Binding capacity (per 10 ul) ranged from 46% at 5 ug down to 8% for 0.00625 ug CEA. The nature of the increased breakdown detected by using decreasing CEA concentrations is difficult to explain. Presently studies are being conducted in adenocarcinomas in which the concentrations of CEA-like substances are low. Therefore, the labeling of satisfactorily purified extracts at low concentrations (Lowry technique) may turn out insufficient to obtain a labeled antigen with an immunological activity such as may be exploited by radioimmunoassay. (17 Refs)

11. RADIOIMMUNOASSAY OF CARCINOEMBRYONIC ANTIGEN.

Krantz MJ, Laferte S, Ariel N
Dept. Medicine, Cross Cancer Inst., Edmonton, Alberta T6G 1Z2, Canada
Methods Enzymol; 84:32-48 1982

Methods for purification of carcinoembryonic antigen (CEA), preparation of antisera, and use of these reagents in a double antibody radioimmunoassay for CEA are discussed. The assay has not been designed for clinical investigations and has not been tested in this application. Physical and chemical properties of CEA are described. The radioimmunoassay has been used to monitor the purification of CEA and cross-reacting antigens, compare the reactivities of different CEA and anti-CEA preparations, evaluate the effects of modifications of the CEA molecule, and compare cross-reacting antigens with CEA. (32 Refs)

12. THE RADIOIMMUNOASSAY OF A CARCINOEMBRYONIC ANTIGEN FRACTION.

Fong S, Betancourt M, Costa H, Moroz S
Instituto de Oncologia y Radiobiologia, Habana, Cuba
Neoplasma; 29(1):9-18 1982

A qualitative and clinical evaluation of a radioimmunoassay for a carcinoembryonic antigen (CEA) fraction in serum is presented. The technique shows cross-reactions with normal organs' extracts lower than 0.05% and a 0.9977 correlation coefficient. The coefficients of variation indicate satisfactory precision. In the clinical study it was found that sensitivity for lung cancer was higher than for colorectal cancer. Specificity for cancer was 98.3%. These results suggest that the CEA fraction employed shows more lung cancer determinants than for digestive cancer. (Author abstract) (33 Refs)

13. AVIDIN AS A PRECIPITANT FOR BIOTIN-LABELED ANTIBODY IN A RADIOIMMUNOASSAY FOR CARCINOEMBRYONIC ANTIGEN.

Clark BR, Todd CW
Div. Immunology, City of Hope Res. Inst., Duarte, CA, 91010
Anal Biochem; 121(2):257-262 1982

Avidin is used in conjunction with polyethylene glycol to coprecipitate biotin-labeled carcinoembryonic antigen (CEA) antibody and the CEA-antibody complex together with biotin-labeled normal serum proteins. The procedure provides a reliable separation technique for a CEA radioimmunoassay. The technique is broadly applicable to assays employing immune precipitation. (Author abstract) (9 Refs)

14. RETENTION OF CARCINOEMBRYONIC ANTIGEN ON SEPHADEX G-50 AND ACRYLAMIDE GEL BUFFER-EXCHANGE COLUMNS.

Haagensen DE, Sawlivich W, Davis S, Zamcheck N
Mallory Gastrointestinal Lab., Mallory Inst. Pathology, Boston City Hosp., 784 Massachusetts Ave., Boston, MA, 02118
Clin Chem; 28(5):1184-1186 1982

We compared the degree of retention of carcinoembryonic antigen on two types of buffer-exchange columns, Sephadex G-50 and acrylamide gel. Both types retained trace amounts of the antigen applied in the form of a perchloric acid extract, as measured by its release into plasma samples subsequently processed through the same columns. Cross contamination, resulting in values falsely high by greater than 1 ug/L, was observed when columns were reused after processing plasma samples with carcinoembryonic antigen concentrations greater than 700 ug/L. (Author abstract) (4 Refs)

15. COMMERCIAL RADIOIMMUNOASSAY KIT FOR MEASUREMENT OF ALPHA-FETOPROTEIN ADAPTED FOR USE WITH DRIED BLOOD SPECIMENS FROM NEWBORNS.

Mizejewski GJ, Bellisario R, Beblowski DW, Carter TP
Birth Defects Inst., Div. Lab. and Res., New York State Dept. Health, Albany, NY, 12201
Clin Chem; 28(5):1207-1210 1982

We adapted a commercial RIA kit to measure alpha-fetoprotein (AFP) in 0.75-uL portions of 60-uL spots of dried blood from newborns. We evaluated sample elution, temperature and time stability, between- and within-assay variability, sensitivity, and use of liquid vs dried specimens of blood. Also, we present normal AFP concentrations for healthy neonates during the first postnatal week. Our procedure permits measurement of AFP concentrations both in maternal liquid plasma and in spots of dried blood from the infant with the same RIA kit reagents and standards. The sensitivity, precision stability, and simplicity of this procedure makes more practical the routine measurement of AFP in dried blood specimens from newborns than measurement in liquid plasma or serum. Blood-sample collection by heel stick suffices for this simple, efficient, inexpensive determination of AFP concentration in the newborn. (Author abstract) (16 Refs)

16. RADIOIMMUNOASAY OF ALPHA-FETOPROTEIN WITH POLYCLONAL AND MONOCLONAL ANTIBODIES.

Ruoslahti E, Uotila M, Engvall E
La Jolla Cancer Res. Foundation, La Jolla, CA, 92037
Methods Enzymol; 84:3-19 1982

Purification of alpha-fetoprotein (AFP) and radioimmunoassay of AFP are described. Measurement of AFP is usually conducted with radioimmunoassay capable of measuring several nanograms of AFP/ml in biological fluids. Because availability of purified AFP is a limiting factor for application the AFP assay, methods available for the preparation of standard AFP are described. Production of monoclonal antibodies to human AFP and the partial characterization of a highly sensitive radioimmunoassay utilizing such antibodies are reported. (29 Refs)

17. ATTEMPT FOR THE EARLY DETECTION OF HEPATOCELLULAR CARCINOMA BY LECTIN-BINDING ANALYSIS OF SERUM ALPHA-FETOPROTEIN (MEETING ABSTRACT)

Endo Y, Miyazaki J, Oda T
First Department of Medicine, University of Tokyo, Tokyo, Japan
Asian Pacific Association for the Study of the Liver and International Association for the Study of the Liver, February 7-12, 1982, Kowloon, Hong Kong. Asian Pacific Association for the Study of the Liver and International Association for the Study of the Liver 110 pp., 1982.

In order to study the significance of lectin-binding analysis of AFP (alpha-fetoprotein) in the eary detection of hepatocellular carcinoma (HCC) and in differentiating it from yolk sac tumor (YST), metastatic liver cancer (Meta) and liver cirrhosis (LC), serum AFP was analyzed by crossed immuno-affinoelectrophoresis. Concanavalin A (ConA) or lens culinaris (LCA) was used as lectin and was cast freely in the first dimension gel (horizontal) at the concentration of 100 ug/cm2. Second dimension gel (vertical) electrophoresis was carried out in the gel containing anti-AFP antibody. Precipitated AFP line was stained with coomassie blue and analyzed. With Con A, AFP was divided into two subfractions (Con A bound and Con A non-bound). Five to ten % of total AFP from HCC and LC were Con A non-bound, whereas 50 to 60 % of total AFP were non-bound in Meta and YST. With LCA, AFP was divided into three subfractions (LCA non-bound, LCA loosely-bound and LCA tightly-bound). AFP in LC was composed mainly of LCA non-bound fraction, whereas different LCA affinity was observed in HCC. In considering these results, lectin-binding analysis of AFP in the serum is considered to be useful in the early detection and the differential diagnosis of HCC. (no Refs)

18. COMPARISON OF PLASMA CEA LEVELS BY THE ROCHE AND ABBOTT METHODS IN BENIGN AND MALIGNANT DISEASES (MEETING ABSTRACT)

Greenberg LJ, Kiang DT
Departments of Laboratory Medicine and Pathology and Medicine, University of Minnesota Medical School, Minneapolis, MN, 55455
Proc Am Assoc Cancer Res; 23:984 1982

Blood carcinoembryonic antigen (CEA) levels have been used in monitoring the clinical course of cancer patients. The two major assay systems, Roche and Abbott, differ both in methodology and antibodies which may produce discrepant results. In order to investigate this problem, CEA levels were assayed in 355 plasma samples from patients with malignant and benign diseases and 234 from normal controls. The controls yielded a mean +/-2SD of less than 3 ng/ml by both methods. In 31 samples from breast cancer patients, CEA levels were normal by one method but elevated by the other. In some occasions, an opposite direction of CEA changes was observed when serial blood samples were examined. Evidence from this study suggests that these two methods yielded comparable results in most instances, however, because of the high frequency of discrepancy, they are probably measuring two or more different antigenic determinants which vary among diseases and during the clinical course of breast cancer. (1 Ref)

19. CHARACTERIZATION OF MONOCLONAL ANTIBODIES TO CARCINOEMBRYONIC ANTIGEN (CEA) (MEETING ABSTRACT)

George S, Ulrich T, Tribby I, Tomita J
Abbott Laboratories, North Chicago, IL, 60064
Fed Proc; 41(3):414 1982

Monoclonal antibodies to CEA were prepared by fusion of CEA-sensitized Balb/c mouse spleen cells with P3 or SP2/0 mouse myeloma cells. Hybridomas producing specific anti-CEA antibodies were propagated as tumors in mice. The Ig fractions from ascites fluids were purified by protein-A Sepharose affinity chromatography. The resulting antibodies were shown to be homogeneous on polyacrylamide gel electrophoresis. A total of five different CEA specific determinants were identified by monoclonal antibodies. Analysis of antibody subtypes by mouse Ig specific antisera showed the presence of Kappa light chain and IgG1 heavy chain. Relative binding affinities of the antibodies were in the range of 10(9) to 10(10) liters/mole (Sip's analysis). Comparison of monoclonal and conventional guinea pig anti-CEA antibodies by competitive inhibition RIA (radioimmunoassay) or solid phase enzyme immunoassay gave nearly identical binding curves. Serum CEA values obtained through the use of monoclonal or guinea pig antibodies in the solid phase enzyme immunoassay system resulted in greater than 99% correlation. (no Refs)

EXPERIMENTS IN ANIMAL SYSTEMS

20. SOLID TUMORS OF HUMAN PRIMARY HEPATOCELLULAR CARCINOMA CELL-LINES IN HYPOTHYMIC MICE: A MODEL FOR BIOCHEMICAL AND THERAPEUTIC STUDIES.

Hahn EG, Gauss-Muller V, Hornberger M, Kalbfleich H, Delahardt F
Medizinische Klinik und Poliklinik, Universitatsklinikum Steglitz, Hindenburgdamm 30, D-1000 Berlin 45, W. Germany
Z Gastroenterol; 20(3):168-173 1982

The behavior of human primary hepatocellular carcinoma (HPHC) cell lines was studied in nude mice. Hypothymic mice of strains Balb/c nu/nu and C57Bl nu/nu were injected sc with 1-8 x 10(7) cells from HPHC lines PLC/PRF/5, Hep3B, or Mahlavu. The first two strains produce hepatitis B surface antigen (HBsAg); Mahlavu cells do not. All three cell lines produced solid tumors that were successfully transplanted sc into additional mice. Significant differences in growth were not noted between cell line. Tumor growth was detectable within 14 days. Retransplantation allowed production of large homogeneous experimental groups and larger tumor masses. No evidence of metastasis was found in lung, liver, or spleen tissue of host animals. Tumors were separated from host tissue by capsules of connective tissue. HBsAg, alpha-fetoprotein (AFP), fibrinogen, and alpha-antitrypain (AAT) were detected by immunofluorescence techniques in cells of PLC/PRF/5 and Hep3B tumor transplants. No positive reactions for hepatitis A or Bc virus antigens were noted. No HBsAg, AFP, fibrinogen, AAT, or hepatitis virus antigens was detected in Mahlavu tumor transplants. Growth of cells exhibiting many of the properties of the original tumors without immunosuppressive treatment of the host animals makes the nude mouse-HPHC model suitable for study of human hepatocellular carcinoma. (6 Refs) (In GER)

21. INHIBITION OF SYNTHESIS OF ALPHA-FETOPROTEIN BY GLUCOCORTICOIDS IN CULTURED HEPATOMA CELLS.

Chou JY, Mano T, Feldman M

Pregnancy Res. Branch, Natl. Inst. Child Health and Human Development, NIH, Bethesda, MD, 20205

J Cell Biol; 93(2):314-317 1982

Alpha-fetoprotein (AFP) synthesis was studied in the presence and absence of glucocorticoids in rat hepatoma Mc-A-RH-7777 cells. Radioimmunoassay of media from cell cultures grown in the presence of glucocorticoid (dexamethasone or cortisol) showed a reduction in AFP, an increase in albumin, and no significant change in transferrin accumulation, as compared to controls. Labeling experiments with L-[35S]methionine indicated that in both cells and media of dexamethasone-treated cultures there was a 50-80% reduction in polypeptide precipitated by anti-AFP serum, as compared with controls; no change was seen in polypeptide precipitated by anti-transferrin serum. Pulse and pulse-chase experiments demonstrated that dexamethasone inhibited the synthesis of AFP but not its secretion. The half-time for secretion of AFP in the presence and absence of dexamethasone was 43 min. (Author abstract) (21 Refs)

22. ALPHA-FETOPROTEIN DYNAMICS DURING ETHIONINE-INDUCED HEPATOCARCINOGENESIS IN RAT.

Miyazaki M, Wahid S, Matsuura K, Watanabe A

Div. Pathology, Cancer Inst., Okayama Univ. Medical Sch., Okayama 700, Japan

Res Exp Med (Berl); 180(2):155-159 1982

The dynamics of alpha-fetoprotein (AFP) during hepatocarcinogenesis induced by DL-ethionine (ET) was studied in adult female Sprague-Dawley rats. Rats were fed a powdered basic diet which contained 0.25% ET throughout the more than 7 mo of the experiment. AFP in the serum and in liver tissue was determined by a radioimmunoassay using the double antibody method. Serum AFP in ET-fed rats reached a max of 1,500 nanog (ng)/ml in wk 6, with subsequent gradual decline to 500 ng/ml between wk 10 and 14. Serum AFP levels then rose to 1,300 ng/ml in wk 22, by which time well-differentiated hepatocellular carcinomas had developed, and then declined markedly. AFP content (ng/g tissue) in ET-induced hepatoma (610) was slightly lower than that in adjacent non-tumorous portions of liver (687). These observations indicate that the hepatocellular carcinoma induced by ethionine does not produce high concentrations of AFP. (13 Refs)

23. THE ROLE OF CELL SURFACE PROTEINS IN THE INDUCTION OF HISTOGENETIC DIFFERENTIATIVE RESPONSES BY SOME HUMAN BREAST TUMOURS AND HAMSTER TUMOURS IMPLANTED INTO CHICK EMBRYOS.

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Exp Cell Biol; 50(3):169-179 1982

Cells of human breast tumors and fibrocystic hyperplasia grown in culture, and three hamster tumors were implanted between the cell layers of 18-hr-old chick blastoderm. Their ability to induce histogenetic responses in the ectodermal and endodermal embryonic tissues was investigated. The surface proteins of these tumor cells were labeled by lactoperoxidase-catalyzed radioiodination. It is shown that the ability to induce the histogenetic effects may be related to the expression of 265K (K = 10(3) daltons) and 233K proteins on the surface of human tumor cells and of 115 K proteins on the hamster tumor cells. The antiproteinase, aprotinin, inhibits the induction of the histogenetic responses by and apparently also prevents the deletion of 115K proteins from the hamster tumor cells. It is therefore suggested that cell surface proteins are involved in the complex processes of interaction between embryonic and tumor cells and in the recognition by the embryonic cells of the tumor cells implanted into their midst. (Author abstract) (23 Refs)

24. SYNTHESIS AND SECRETION OF ALPHA-FETOPROTEIN AND ACUTE-PHASE ALPHA2-MACROGLOBULIN BY ZAJDELA RAT ASCITES HEPATOMA.

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Oncodev Biol Med; 3(1):23-29 1982

Zajdela rat ascites hepatoma cells have been reported to be 'nonsecretors' of alpha-fetoprotein (AFP). Because of the potential of such cells in the study of defective secretory mechanisms of AFP and other serum proteins, we conducted a detailed investigation of the production of AFP in Zajdela cells growing in vivo. Three approaches were used: radioimmunoassay of intracellular and extracellular AFP and assays of AFP mRNA by molecular hybridization and cell-free translation. Radioimmunoassay showed that the AFP concentration in the hepatoma cells was extremely low (1.2 ug/g) as compared to known AFP-producing tissues such as fetal liver (600 ug/g). The assays of AFP mRNA by hybridization and translation supported the low level of AFP production in Zajdela cells, and we consider such cells to be poor producers of AFP and therefore not suitable for the study of defective mechanisms for AFP secretion. The Zajdela tumor cell intracellular concentration of acute-phase alpha2-macroglobulin (APalpha2M) measured by radioimmunoassay was also found to be low (3.0 ug/g) compared to liver of Zajdela-bearing rats (80 ug/g). In view of these low levels of synthesis of AFP and APalpha2M in Zajdela hepatoma cells, little biological significance may be attached to the apparent nonsecretion of these onco-fetal proteins. (Author abstract) (13 Refs)

25. ROLE OF ALPHA-FETOPROTEIN (AFP) IN THE REGULATION OF OVARIAN ACTIVITY DURING HEPATOCARCINOGENESIS AND POST-NATAL DEVELOPMENT.

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Oncodev Biol Med; 3(1):65-71 1982

N-2-fluorenylacetamide produces an augmentation of serum AFP which is accompanied by a drastic decrease of ovarian activity. A passive augmentation of the AFP levels of adult rats, produced by injection of this protein provokes the same phenomenon: ie a decrease of follicular maturation, a decreased number of corpora lutea and finally a drop in the plasma progesterone level. The study of ovarian post-natal development shows that ovarian maturity occurs on the 35th day of life when AFP level reaches its adult serum concentration. These facts support the hypothesis that AFP plays a role in the regulation of ovaries during the sexual maturation of the female rat. (Author abstract) (19 Refs)

26. EFFECT OF HEPATOCYTE PROLIFERATION AND NEOPLASTIC TRANSFORMATION ON ALPHA-FETOPROTEIN (AFP) AND ALBUMIN (ALB) PRODUCTION PER CELL. INFLUENCE OF CELL SPECIALIZATION AND CELL SIZE.

Marceau N, Deschenes J, Valet JP
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Oncodev Biol Med; 3(1):49-63 1982

Hepatocytes were isolated from 2-day regenerating livers of 21-day- and 12-wk-old rats, and the percentage of cells specialized in AFP and ALB production was evaluated using the reverse hemolytic plaque assay. In comparison to the data obtained with hepatocytes from non regenerating livers, the percentage of ALB producers was not significantly modified during the regenerating process; the percentage of AFP producers at 23 days of age went from a non detectable level to 5% while at 12 wk it remained at an extremely low value. Double identification of secreting hepatocytes further revealed that the re-occurring AFP producers were recruited among those already producing ALB. The isolated hepatocytes were also fractionated according to size by velocity sedimentation at 1 x g and the actual production rate of AFP and ALB was determined on a per cell or a per mg protein basis. Again, regeneration process did not alter the ALB production rate, whereas AFP became detectable only with hepatocytes from 23-day-old rats. The same approach was used to evaluate the relationship between AFP/ALB specialization versus cell size for Morris 7777 and 7795 and Novikoff hepatoma cells. The results showed that on a per mg basis, after correction for the percentage of specialized cells, Morris 7777 cells produced AFP at a rate comparable to that of the normal neonatal hepatocytes. Both Morris 7777 and 7795 hepatoma cells produced ALB at a low rate. Novikoff hepatoma cells produced no detectable amount of the two exportable proteins. The analysis by velocity sedimentation at 1 x g also revealed that the three hepatoma cell lines were essentially identical in size. They were found to be smaller than neonatal hepatocytes but comparable in size to hepatic epithelial cells that can be isolated from normal rats and propagated in culture. These results are discussed in terms of proposals suggesting that hepatic epithelial cells may correspond to precursors or stem cells of hepatocytes and to target cells during chemical hepatocarcinogenesis. (Author abstract) (56 Refs)

27. EXPRESSION AND METHYLATION OF THE MOUSE ALPHA-FETOPROTEIN GENE IN EMBRYONIC, ADULT, AND NEOPLASTIC TISSUES.

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J Biol Chem; 257(9):5148-5153 1982

Expression of the mouse alpha-fetoprotein gene in embryonic, adult, and neoplastic tissues was assessed by RNA dot hybridization using 32P-labeled alpha-fetoprotein cDNA as probe. Alpha-fetoprotein mRNA was present in high levels in total RNA from yolk sac endoderm, fetal liver, and an alpha-fetoprotein-producing hepatoma. In contrast, this mRNA was greatly depleted in total RNA from yolk sac mesoderm and essentially absent in brain, adult liver, and a non-alpha-fetoprotein-producing hepatoma. These results indicated that alpha-fetoprotein gene expression was controlled primarily at the transcriptional level. The presence of the modified base, 5-methylcytosine, in the alpha-fetoprotein gene was studied by comparing hybridization patterns obtained by Southern blot analysis of DNA cleaved with the restriction isoschizomers endonuclease Msp I and endonuclease Hpa II. The gross sequence organization and reiteration frequency of the alpha-fetoprotein gene were invariant among the DNA samples, whereas, in each case, there was a positive correlation between hypomethylation of six CCGG (Hpa II) sites in the alpha-fetoprotein gene and expression of this gene. These Hpa II sites were distributed throughout a large portion of the alpha-fetoprotein gene. Patterns of cytosine methylation in this gene were established before day 15 of gestation in yolk sac endoderm and mesoderm. (Author abstract) (46 Refs)

28. A NEW KUPFFER CELL RECEPTOR MEDIATING PLASMA CLEARANCE OF CARCINOEMBRYONIC ANTIGEN BY THE RAT.

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Biochem J; 204(2):377-381 1982

Native human carcinoembryonic antigen is rapidly removed from the circulation by the rat liver Kupffer cells after intravenous injection. The molecule is subsequently transferred to the hepatocyte in an immunologically identifiable form. Carcinoembryonic antigen has a circulatory half-life of 3.7 (+-0.8)min, and cellular entry is by receptor-mediated endocytosis. Non-specific fluid pinocytosis and phagocytosis can be excluded as possible mechanisms by the kinetics of clearance and failure of colloidal carbon to inhibit uptake. Substances with known affinity for the hepatic receptors for mannose, N-acetylglucosamine, fucose and galactose all fail to inhibit carcinoembryonic antigen clearance. After two cycles of the Smith degradation, carcinoembryonic antigen is still able to inhibit clearance of the native molecule. Receptor specificity is apparently not dependent on those non-reducing terminal sugars of the native molecule. Performic acid-oxidized carcinoembryonic antigen also inhibits clearance of carcinoembryonic antigen in vivo. Receptor binding is not dependent on tertiary protein conformation. Non-specific cross-reacting antigen, a glycoprotein structurally similar to carcinoembryonic antigen, is cleared by the same mechanism. (Author abstract) (30 Refs)

29. IDENTIFICATION OF ANTIBODIES TO HUMAN PANCREATIC CANCER CELLS IN IMMUNOCOMPETENT HAIRY LITTER MATES IMMUNIZED WITH SERUM FROM TUMOUR-BEARING NUDE MICE (MEETING ABSTRACT)

Grant AG, Duke D, Hermon-Taylor J
Department of Surgery, St. George's Hospital Medical School, London, England
Br J Cancer; 44(2):298 1981

Using the concept that tumor cells synthesize and release specific membrane-associated proteins during growth, antibodies have been raised in immunocompetent hairy litter mates to sera from nude mice bearing human pancreatic tumor. No antibodies were detected in tumor-bearing nude-mouse serum. Antisera raised against sera from 2 different pancreatic cancer xenografts showed a titer of activity greater than 1.625 against cultured pancreatic tumor cells by an I125-binding assay. Five out of the 14 hairy litter mates immunized with serum from the same tumor (GER) produced antisera that bound more strongly to pancreatic cancer cells (binding ratio greater than 2) when tested against human fetal pancreatic fibroblasts, normal and EBV-(Epstein-Barr Virus) transformed lymphocytes, myeloid, lymphoblastoid, mammary and urinary bladder human tumor cell lines, and a murine tumor cell line. Binding ratios of less than 2 were found with a fibroblast cell line derived from the same pancreatic tumor (GF) and a colon tumor cell line HT-29. Adsorption of the antisera with CEA (carcinoembryonic antigen) reduced the level of binding by 11-24% without affecting the specificity for pancreatic tumor cells. Immunofluorescent staining of pancreatic tumor sections indicated that the antibody was localized on the membrane of ductular epithelial cells. Challenge of immunocompetent mice using this procedure may provide a route to the production of antibody for the characterization of selected tumor components. (no Refs)

30. EFFECT OF IMMUNIZATION OF RATS WITH HUMAN ALPHA-FETOPROTEIN (AFP) UPON THE DEVELOPMENT OF HEPATOMA BY 3'-METHYL-4-DIAMINOAZOBENZENE (MEETING ABSTRACT)

Yamazaki Y, Sato K, Taga H, Ishizuka H, Kaneda H, Honda T
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Asian Pacific Association for the Study of the Liver and International Association for the Study of the Liver, February 7-12, 1982, Kowloon, Hong Kong. Asian Pacific Association for the Study of the Liver and International Association for the Study of the Liver 110 pp., 1982.

It has been demonstrated that the administration of anti-rat AFP horse serum inhibited the elevation of serum AFP and the development of hepatoma by 3'-Me-DAB (3'-methyl-4-diaminoazobenzene) (passive immunization). It has also been known that when animals are immunized with AFP which is heterologous to that animal, they produce antibodies both to the heterologous AFP and to their own AFP (active immunization). In this study rats were immunized with human AFP and its effect upon serum AFP levels and development of hepatoma by 3'-Me-DAB was investigated. Rats immunized with 0.5 mg human AFP with Freund's complete adjuvant produced the antibody both to human and rat AFPs, the titers of which were 8-64 times and 2 times respectively. These rats were fed 3'-Me-DAB containing diet. At the time of hepatoma development 8 out of 10 control rats showed elevated serum AFP levels, and died of tumor in 21 weeks. On the other hand, in the immunized rats only 2 out of 6 showed elevated AFP and died of tumor. But 4 rats maintained low AFP levels and survived. No tumor was detected in survived rats which were sacrificed in the 30th week. (no Refs)

31. EFFECT OF A CONJUGATE OF DAUNOMYCIN WITH A HORSE ANTIBODY TO RAT ALPHA-FETOPROTEIN ON THE GROWTH OF RAT HEPATOMA CELLS (MEETING ABSTRACT)

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Asian Pacific Association for the Study of the Liver and International Association for the Study of the Liver, February 7-12, 1982, Kowloon, Hong Kong. Asian Pacific Association for the Study of the Liver and International Association for the Study of the Liver 110 pp., 1982.

The cytotoxic activity of specific antibody to alpha-fetoprotein (AFP) on AFP-producing tumor was demonstrated both in vitro and in vivo. The aim of this study was to test specific cytotoxic activity of the conjugate of an anti-rat AFP horse antibody and daunomycin. Specific antiserum to rat AFP was produced in horses. The specific antibody was purified by affinity chromatography on Sepharose-4B coupled to rat AFP. Then, the specific antibody was linked covalently to daunomycin via a dextran bridge. The pharmacological and antibody activities of the conjugate were measured by the inhibition of DNA synthesis and radioimmunoassay respectively. A rat ascites hepatoma cell line, AH66 was used for in vitro and in vivo studies. The specific cytotoxicity of the conjugate and various controls was assessed by the inhibition of cell growth in vitro. Marked cytotoxicity was observed in the vials to which the conjugate was added. The results indicated that the conjugate retains sufficiently both drug and antibody activity. The therapeutic effect of the conjugate was evaluated by testing its ability to prevent the in vivo development of tumors. The conjugate showed a higher inhibitory effect on the tumor growth than that of daunomycin or antibody alone and a simple mixture of both. (no Refs)

32. HETEROTRANSPLANTED HUMAN TUMORS LOCATED BY A RADIOLABELED MONOCLONAL ANTIBODY (ANTI-SSEA-1) (MEETING ABSTRACT)

Ballou B, Reiland JM, Levine G, Solter D, Taylor RJ, Hakala TR
University of Pittsburgh, Pittsburgh, PA, 15261
Fed Proc; 41(3):555 1982

Stage-Specific Embryonic Antigen I (SSEA-1), originally discovered on murine teratocarcinomas, has since been found on some human non-seminomatous germ-cell tumors and adenocarcinomas (eg colonic carcinoma; renal adenocarcinoma), as well as on some adult murine and human tissues. A monoclonal antibody to the antigen (anti-SSEA-I; IgM,k) was radiolabeled using 131-I and co-injected with a 125-I labeled unselected myeloma protein of the same class (MOPC 104E) into nude mice bearing the human choriocarcinoma BeWo, which is SSEA-I positive. Animals were sacrificed at 24-hr intervals; appropriate organs and tissues were removed, weighed, and counted to follow the relative concentrations of both antibodies in the tumor and various organs. Accumulation of the anti-SSEA-1 in the tumor was consistently rapid and specific, while no accumulation of the unselected myeloma protein occurred. No accumulation in normal mouse tissues was found. At five days after injection, an average of 3% of the initial dose of specific antibody was retained per gram of tumor; the tumor/muscle ratio was 80, tumor/blood 11. Gamma-camera imaging allowed ready location of the tumors. (no Refs)

33. IDENTIFICATION AND PURIFICATION OF A RECEPTOR FOR TUMOR ASSOCIATED FETAL ANTIGENS (MEETING ABSTRACT)

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Fed Proc; 41(3):414 1982

Tumor associated fetal antigens (TAFA) are immunosuppressive low molecular weight proteins that share many molecular properties with interleukin-1. TAFA have pI (isoelectric point) heterogeneity; a molecular weight (MW) range of 12,000-17,000; and TAFA have been shown to suppress human and murine natural killer cell activity. In the present study, binding by TAFA-II to NBR rat spleen cells was shown to be reversible and saturable; and at equilibrium, affinity measurements revealed a moderate binding association constant of 2.4 x 10(6)/M. Normal spleen cells were treated with 125I-TAFA-II and then solubilized with 0.5% NP-40. The labeled and solubilized membrane extracts were analyzed by G-100 Sephadex chromatography. A complex with a MW of 90,000 was isolated and analyzed by isoelectric focusing. The 125I-TAFA-II/receptor complex was next immuneprecipitated with anti-TAFA-II. In the presence of TAFA-II and anti-TAFA-II, the purified receptor was immuneprecipitated and analyzed in 10% SDS-PAGE (sodium dodecyl sulfate-polyacrylamide gel electrophoresis). Analysis of the dissociated complexes demonstrated the presence of a purified receptor (MW 65,000-75,000d). Using lentil lectin chromatography the receptor was found to be a mannose containing glycoprotein. These data indicate that receptor binding by TAFA is specific, and that the immunoregulatory effects of TAFA depends on direct interactions with immunocompetent cells. (no Refs)

34. STUDIES ON RAT CARCINOEMBRYONIC ANTIGEN (CEA) (MEETING ABSTRACT)

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Fed Proc; 41(3):412 1982

Rat CEA was recently described in our laboratory in perchloric acid (PCA) extracts of rat colon tumors that had been induced with dimethylhydrazine. This study showed that rat CEA is similar to human CEA in physicochemical properties and tissue distribution. This rat model was used to study the immunogenicity of CEA in a syngeneic host. CEA-containing rat tumors grown in Fischer rats were extracted with saline. Syngeneic rats were immunized with the saline extracts incorporated into complete Freund's adjuvant (CFA). Sera from these rats were tested by an enzyme immunoassay using microtiter plates with wells coated with rat CEA. The sera from 32 of 34 immunized rats contained antibodies that bound to rat CEA. No binding was observed in wells coated with PCA extract of normal rat tissue. Pre-immune sera and sera from rats immunized with CFA alone gave negative results in the assay. Antibody activity was completely inhibited by PCA extracts of rat colon tumor but not of normal rat tissue including colon, liver, kidney or serum, even at high concentration. Interestingly, when PCA rather than plain saline extract of CEA was used there was hardly any antibody response. Experiments are in progress to determine the effectiveness of the anti-rat CEA response in preventing tumor growth and/or causing regression of a growing tumor in rat. (1 Ref)

35. ANTIBODIES TO A TUMOR ASSOCIATED ANTIGEN COPURIFYING WITH A TUMOR SPECIFIC TRANSPLANTATION ANTIGEN (MEETING ABSTRACT)

Riley LB, Kahan BD, Pellis NR
The University of Texas Health Science Center Medical School, Houston, TX, 77030
Fed Proc; 41(3):311 1982

The tumor specific antigens of methylcholanthrene (MCA) induced neoplasms seldom engender humoral immunity in syngeneic or autochthonous hosts. Antibodies to tumor specific or tumor associated antigens were sought by inoculation of a H-2Kk variant C3HfeB/HeN (H-2Kkvl) with cells from the MCA induced fibrosarcoma (MCA-F) of C3H/HeJ origin. Following rejection of a 1 cm neoplasm and 6 subsequent boosts with irradiated MCA-F cells, sera were assessed for antibodies to MCA-F antigens using an enzyme linked immunosorbent assay. The C3H/f antisera bound significantly more to isoelectrically purified TSTA than to KCl extracts of either C3H/HeJ spleen cells or embryonic tissue. A panel of five monoclonal anti gp-70 as well as two polyclonal anti-H-2Kk antisera reacted significantly greater with spleen cell embryonic tissue extracts than with purified TSTA, demonstrating that this antiserum detects antigens other than H-2Kk and gp-70. Finally the C3H/f antisera reacted with a 161,000 mw component of isoelectrically focused TSTA from gel permeation chromatography. This component did not have significant reactivity with either the anti-H-2Kk nor the anti-gp-70 antibodies. These results suggest that C3H/f antiserum detects a 161,000 mw tumor associated antigen that is neither H-2Kk nor gp-70 related and copurifies with the known TSTA. (no Refs)

36. RETINOIC ACID BINDING PROTEIN IN NORMAL AND NEOPLASTIC RAT PROSTATE.

Gesell MS, Brandes MJ, Arnold EA, Isaacs JT, Ueda H, Millan JC, Brandes D
(c/o Isaacs) James Buchanan Brady Urological Inst., Johns Hopkins Hosp., Marburg Building, 600 N. Wolfe St., Baltimore, MD, 21205
Prostate; 3(2):131-138 1982

Cytosolic retinoic acid-binding protein (cRABP) was detected, using sucrose density gradient centrifugation, in four sublines of the Dunning R 3327 transplantable prostatic carcinoma and in the normal lateral prostate of the Fisher-Copenhagen F1 rat; cRABP was not detected in the dorsal lobes (the tissue of origin of R 3327 in a Copenhagen rat) or ventral prostate. The presence of cRABP in all four R 3327 tumor sublines, which differ in their degree of differentiation and hormone responsiveness, suggests that cRAPB may be a marker of malignant transformation similar to other oncofetal proteins in human and animal tumors. (40 Refs)

IMMUNOLOGIC INTERACTIONS

37. PRELIMINARY IMMUNOLOGICAL EVALUATION OF CARCINOMA OF THE BREAST AND THYROID GLAND.

Abeatici S, Mussa A, Levis P, Sandrucci S, Storta P
Istituto di Clinica Chirurgica II, Universita di Torino, Turin, Italy
Minerva Med; 73(18):1149-1154 1982

Immunological parameters were studied preoperatively and postoperatively in 15 women with malignant tumors (7 with thyroid lesions of the thyroid or of the breast). The total percentage of leukocytes and E rosettes showed a significant difference between the cancer patients and controls and was not affected by surgery. The percentage of B lymphocytes was higher in the cancer patients (2-70%, av 16.4%) than in the controls (4-20%, av 8.1%). The corresponding percentages after surgery were 12.8% and 6%, respectively. The cortisol levels were 100-400 nanog (ng)/ml for cancer patients and 100-250 ng/ml for controls. The mean values were 217.6 ng/ml for cancer patients vs 157.5 ng/ml for controls. The carcinoembryonic antigen (CEA) levels measured before surgery were significantly higher for the patients with thyroid carcinoma than for the patients with goiter. Significant reduction of CEA level was seen after surgery in the cancer patients compared with the preoperative levels. CEA levels were lower in the patients with breast cancer than in those with thyroid carcinoma, and did not differ to much from those measured in the patients with benign breast lesions. CEA levels of the breast cancer patients decreased to 2-3 ng/ml after a slight transient rise shortly after surgery. The IgA, IgG and IgM levels in the patients with thyroid carcinoma were higher than in the patients with benign thyroid lesions. Surgery caused no significant changes in the immunoglobulin levels. (22 Refs) (In ITA)

38. EFFECT OF CEA PRODUCTION ON THE SENSITIVITY OF HUMAN TUMOR CELLS TO LYSIS BY NATURAL KILLER CELLS (MEETING ABSTRACT)

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Proc Am Soc Clin Oncol; 1:C-136 1982

Addition of BCG to combination chemotherapy (5-fluorouracil + cyclophosphamide + adriamycin) in our patients with advanced breast cancer produces significant benefit only in the subgroup of patients who have the fetal antigen CEA (carcinoembryonic antigen) elevated in their pre-therapy plasma samples. BCG therapy had no consistent effect on the response to DNCB (dinitrochlorobenzene), recall antigen skin tests, or in vitro response to PHA (phytohemagglutinin). Since BCG therapy may augment the activity of natural killer cells, we have tested different clones derived from an adenocarcinoma cell line that release different amounts of CEA into their supernatant to determine if CEA production correlates with sensitivity to lysis by NK cells. A high CEA-producing line of HCT-8 cells proved significantly more sensitive to lysis in a 20 hr 51 Cr-release assay than did a low CEA-producing line. Saturation of the assay with alpha-interferon or addition of anti-interferon antibody to the assay did not eliminate the difference in sensitivity to lysis, and mixing experiments confirmed that the higher sensitivity to lysis by the CEA producing line was not due to induction of NK activity. Limiting dilution analysis showed that the high CEA line reacted with a much larger population of blood NK cells. A greater proportion of NK cells killing high CEA line cells were E rosette positive. Theophyline induced enhancement of expression of surface CEA-like antigen was associated with an increase in sensitivity to lysis by NK cells. (no Refs)

CLINICAL/ DIAGNOSIS/ IMMUNOTHERAPY

39. THE DIAGNOSIS OF CANCER THROUGH THE SYSTEMATIC MONITORING OF SERUM CARCINOEMBRYONIC ANTIGEN IN A DEPARTMENT OF INTERNAL MEDICINE.

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Rev Med Liege; 36(3):106-110 1981

In a series of 434 patients whose serum levels of carcinoembryonic antigen (CEA) were tested, 364 had noncancerous diseases. In this group, 324/364 (89%) had normal levels of CEA. Questionable levels of CEA were present in 26 patients (7%) and 14 patients (4%) had abnormal CEA levels. Among the 70 patients with cancer, 35 (50%) had normal CEA levels, 9 (13%) had questionable levels of CEA and 26 (37%) had abnormal CEA levels. The sites of the primary tumor in patients with abnormal CEA included sigmoid colon (7), pancreas (3), prostate (1), breast (1), lungs (5), brain (1), bladder (1), and rectum (1). The high number of false negative (50%) discredited the method as a means at early diagnosis. When the CEA levels were questionable or abnormal, cancer was discovered in 35/74 (47%) cases. In advanced cases, more than half of the patients (19/35) had abnormal levels of CEA. In 7/12 rectosigmoid and in 4/9 pancreatic cancers, when was discovered the cancer was generalized. Abnormal levels of CEA were found in 6/10 lung cancers in which metastases would not have been detected by other methods. (31 Refs) (In FRE)

40. PRIMARY LIVER CANCER IN THE TRANSVAAL.

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Hepatogastroenterology; 28(5):233-235 1981

The clinical picture of 60 cases of primary liver cancer is reported. Distended abdominal veins found in a substantial number of cases, often point to collateral circulation due to a membrane in the inferior vena cava (Budd-Chiari syndrome). Alpha-fetoprotein, alkaline phosphatase and gamma-glutamyltranspeptidase were the only reliable laboratory pointers to the disease. Ultrasound study proved to be very helpful. Thrombocytopenia was found in 5 out of 12 of our patients. (Author abstract) (8 Refs)

41. ALPHAFETOPROTEIN LEVELS MEASURED BY RADIOIMMUNOASSAY IN VARIOUS LIVER MALIGNANCIES.

Chang FY, Chen TC, Fong MS, Lin S, Yeh SH
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Taiwan I Hsueh Hui Tsa Chih; 81(2):224-231 1982

Alpha-fetoprotein (AFP) levels in 114 patients with primary hepatocellular carcinoma (HCC), 11 patients with cholangiocarcinoma, and 17 patients with metastatic liver cancer were determined by radioimmunoassay, and compared with similar determinations in 44 adults with normal liver function. AFP levels in the healthy subjects never exceeded 20 nano(n)g/ml; 39 determination were less than 10 ng/ml. Of the 142 cancer patients, 93/114 HCC, 3/11 cholangiocarcinoma, and 2/17 metastatic liver cancer patients had AFP levels greater than 20 ng/ml. Rates of elevation of AFP in cancer patients seemed to decrease with increasing patient age, but the relationship as not statistically significant. Among 75 hepatitis B surface antigen

(HBsAG)-positive patients, 86.7% had AFP levels greater than 20 ng/ml. Of 15 HBsAg-negative HCC patients, 66.7% had AFP levels greater than 20 ng/ml. The relation of HBsAg-positivity to elevated AFP level was not statistically significant. More than half of the HCC patients had AFP level greater than 320 ng/ml, but not all HCC patients had elevated AFP due to lower secretion. The relationship of HCC to HBsAg-positivity may be causal in this Taiwanese population, in which both hepatitis B infection and HCC are common. (32 Refs)

42. LAPAROSCOPIC EXAMINATION OF CHRONIC LIVER DISEASES: POSSIBLE RELATIONSHIP BETWEEN PATCHY MARKING AND HEPATOCELLULAR CARCINOMA.

Numa Y, Fukumoto Y, Esaki T, Oda M, Ando K, Tsubota W, Miyazaki M, Morimoto T, Matsuda S, Watanabe S, Kodama T, Okita K, Takemoto T

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Gastroenterol Endosc; 23(6):808-813 1981

The relationship between red spot patchy marker (patchy marker) and hepatocarcinoma (HCa), and between hepatitis B surface antigen (HBsAg)-hepatitis B surface antibody (HBsAb) system and morphology of lymph nodes by laparoscopic observation was investigated in 103 patients with chronic liver diseases (CLD) and 25 patients with HCa. Patchy marker was detected in 30/103 (29.1%) CLD patients: 1/15 (6.7%) with chronic non-active hepatitis, 15/50 (30%) with chronic active hepatitis, and 14/38 (36.8%) with liver cirrhosis. Twenty-three (22.3%) of 103 CLD patients had liver cell dysplasia. Of 100 CLD patients tested, HBsAg was positive in 26, and HBsAb was positive in 12. Patients without patchy marker showed a higher frequency of being positive for either HBsAg or HBsAb than those with patchy marker. In contrast, a higher value of alpha-fetoprotein was found more often in patients with patchy marker than in those without patchy marker. Of 21 HCa patients, 4 were positive for HBsAg and none for HBsAb. Patchy marker was positive in 8/21 HCa patients, 2 of whom were positive for HBsAg; patchy marker was negative in 13/21 HCa patients, 2 of whom were positive for HBsAg. These results suggest that such laparoscopic findings may be useful for identifying CLD patients at high risk for developing cancer. (16 Refs) (In JPN)

43. AN APPROACH TO THE DIAGNOSIS OF SUBCLINICAL LIVER CANCER.

Yang B, Lin C, Tang Z

Dept. Liver Cancer Res., Zhongshan Hosp., Shanghai First Medical Coll., Shanghai, People's Republic of China

Zhonghua Xiaohua Zazhi; 1(2):101-103 1981

Diagnostic findings and treatment are described for 81 patients with subclinical liver cancer who showed no cancer symptoms or physical signs. There were 76 men and 5 women, 21 to 66 yr old. All had been detected by alpha-fetoprotein determination, with 71 cases through mass screening for liver cancer and 10 cases during follow-up of hepatitis or liver cirrhosis. Selective hepatic angiography was found to be helpful in the diagnosis. (9 Refs) (In CHI)

44. CLINICAL SIGNIFICANCE OF HYPER-ALPHAFETOPROTEINEMIA IN PATIENTS WITH LIVER DISEASES. AN OBSERVATION OF 483 CASES.

Yuan A, Liu W, Jin H, Luo Y
Dept. Internal Medicine, Affiliated First Hosp., Third Military Medical Coll., Chongqing, People's Republic of China
Zhonghua Xiaohua Zazhi; 1(2):98-100 1981

Alpha-fetoprotein (AFP) determination is now widely used in the mass screening and diagnosis of liver cancer. Results of AFP determination are described for 483 cases of liver diseases that included acute and chronic hepatitis and liver cirrhosis. The overall AFP-positive rate in this series was 23% with most of the AFP values under 200 nanog/ml as opposed to over 200 nanog/ml for primary hepatic cancer patients who are about 80% AFP-positive. Differential diagnosis is discussed. (7 Refs) (In CHI)

45. NONINVASIVE DIAGNOSIS OF PRIMARY HEPATIC TUMORS. VALUE OF DETERMINATION OF AFP COMBINED WITH HEPATIC SCINTIGRAPHY.

Pisitano G, Tesauro P, Siniscalchi A, Di Simone A
Servizio di Endoscopia Digestiva, Universita di Napoli, Naples, Italy
Fegato; 27(3):207-211 1981

Forty patients (27 men and 13 women, 25-70 yr old) with hepatocellular carcinoma diagnosed by biopsy, laparoscopy or both were subjected to hepatic scintigraphy and to alpha-fetoprotein (AFP) test. The AFP levels were pathologically elevated (above 10 ng/ml) in 80% of all patients, and in 67% were above 100 ng/ml. The liver scans showed definite space-occupying lesions in 85% of all patients and a patchy distribution of the radioisotope as seen in chronic liver disease, eg, in cirrhosis, in the other. Both the liver scans and the AFP tests were positive in 97% of all patients, ie, it was possible to establish the correct diagnosis by the combination of the two methods in 97% of the patients. (19 Refs) (In ITA)

46. BENIGN LIVER TUMORS.

Foster JH
Dept. Surgery, Univ. Connecticut Sch. Medicine, Farmington, CT, 06032
World J Surg; 6(1):25-31 1982

New methods, such as ultrasonography, computed tomography, and angiography, are leading to the discovery of more benign liver tumors, which include bile duct adenoma, cystic tumors, hemangiomas, focal nodular hyperplasia, liver cell adenoma, and miscellaneous tumors. Biologic markers such as alpha-fetoprotein and carcinoembryonic antigen may be useful in the detection of some tumors. Drainage is indicated in the larger cystic tumors and resection in symptomatic solid tumors and cystadenomas. (12 Refs)

47. PLASMA PROTEIN PROFILES AND PROGNOSIS IN GASTRIC CANCER.

Rashid SA, O'Quigley J, Axon AT, Cooper EH
Unit Cancer Res., Univ. Leeds, Leeds, England
Br J Cancer; 45(3):390-394 1982

In 104 patients with gastric cancer the serum proteins carcinoembryonic antigen (CEA), C-reactive protein (CRP), alpha 1-acid glycoprotein (AGP) (orosomucoid) and alpha1-antichymotrypsin (ACT) were measured pre-operatively. The estimated median survival of patients with both raised CEA and ACT was only 5 weeks in contrast to 64 wk for those with both proteins normal. An intermediary group with one of these proteins raised and the other normal had an estimated median survival of 15 wk. Similar results were obtained by considering a combination of CEA with either AGP or CRP. For these data the results were not explicable in terms of associations between survival time and patient's age, stage, operative procedure, histological classification or site of primary tumor. (Author abstract) (28 Refs)

48. THE DIAGNOSIS OF PANCREATIC CANCER.

Moossa AR, Dawson PJ
Dept. Surgery, Univ. Chicago, Chicago, IL, 60637
Pathobiol Annu; 11:299-335 1981

Clinical diagnosis of pancreatic cancer (PC), glucose intolerance and PC, the relationship between pancreatitis and PC, selection of patients for investigation, routine blood tests and radiological procedures, pancreatic function tests and imaging techniques, comparison of tests and a rational sequence of testing for PC, diagnosis of early PC, value of tumor markers in diagnosis, diagnosis of incurable PC, and surgical and histological diagnosis of PC are discussed. A survey of literature indicates that 20-60% of patients with PC have some form of glucose intolerance. Endoscopic retrograde pancreatography, ultrasonography, computed tomography, selective abdominal angiography, and radionuclide pancreatic scans have all been evaluated for diagnosis of PC. According to prospective studies on the diagnostic yield of these various methods indicate that ultrasonography was recommended as the initial test for any patient with suspected PC. Results of carcinoembryonic antigen (CEA) measurements in sera of 808 patients with histologically confirmed malignant disease, including 526 patients who had malignant tumors of the gastrointestinal tract were reviewed. Eighty-three percent of PC patients had an elevated CEA level as did 65% of other cancer patients, and 46% of patients with benign disease. Advanced PC can be often diagnosed after careful history and routine physical examination. Twenty-one patients who survived longer than 3 yr following resection for ductal adenocarcinoma of the pancreas were followed. Four of these patients died of primary lung cancer and seven died of cerebrovascular accident or myocardial infarction, all associated with excessive cigarette smoking. (65 Refs)

49. DIAGNOSIS OF PANCREATIC CANCER BY PANCREATIC ONCOFETAL ANTIGEN (POA) IN PURE PANCREATIC JUICE.

Nishida K, Kondo M, Jessen K, Classen M
First Dept. Medicine, Kyoto Prefectural Univ. Medicine, Kamikyoku, Kyoto, 602, Japan
Hepatogastroenterology; 28(2):102-105 1981

Pancreatic oncofetal antigen (POA) was detected in the pure pancreatic juice by double immunodiffusion assay in a series of patients, using anti-POA prepared by immunizing rabbits with human fetal pancreas homogenate. The test was positive in as many as 72% of the patients with pancreatic cancer studied, whereas only less than 10% of patients with other diseases or normal controls were positive for this antigen, thus suggesting a potential usefulness of the pure pancreatic juice assay for POA in the diagnosis of cancer of the pancreas. The POA has proven to be distinct from such oncofetal antigens as AFP and CEA, to be labile to heating at 85 C, to show beta-mobility on immunoelectrophoresis and to have a mol wt of approx 37,000 as estimated by gel filtration chromatography. (Author abstract) (12 Refs)

50. FOLLOW-UP PROCEDURE FOR COLORECTAL CANCER.

Metzger U, Schneider K, Buchmann P, Largiader F
Chirurgische Klinik A, Universitatsspital, CH-8091 Zurich, Switzerland
Praxis; 71(8):327-331 1982

Follow-up care of patients with colorectal cancer (CRC) is discussed and a specific program proposed. Follow-up care should be provided by the family doctor with the goal of early detection and curative treatment of recurrent tumor or metastases. Advantages of follow-up care in general include early detection, the chance of curative treatment, 'quality control' of therapy, and provision of care and support for the patient. Disadvantages include the cost of many procedures, burden to the patient, and psychological problems. Diagnosis of recurrence must take into account possible recurrence in the areas of intestinal anastomosis or colostomy, lymphatic metastases, and metastases in other organs. Basic diagnostic techniques include history taking, digital examination, occult blood tests of feces, measurement of carcinoembryonic antigen (CEA), and laboratory tests. Additional studies include conventional x-rays, hepatic scintigraphy, and ultrasonography. Special studies include coloscopy and rectoscopy. Studies should be performed only when the possibility of therapeutic gain is present. The proposed schedule of follow-up care makes the most effective use of the various study methods to improve detection while minimizing costs and the burden to the patient. (16 Refs) (In GER)

51. CEA-LIKE SUBSTANCES IN BREAST CANCER. DIFFERENCES IN CEA-LIKE ACTIVITY IN 48 PRIMARY BREAST CARCINOMAS.

Accinni R, Ballo M, Cavalca V, Ferrara R, Biancardi C, Bartorelli A
Istituto di Ricerche Cardiovascolari, c/o Centro Cardiologico, Via Bonfadini, 214-20138 Milano, Italy
Boll Ist Sieroter Milan; 60(6):494-497 1981

Carcinoembryonic antigen (CEA) and CEA-like activity was compared in 48 primary breast carcinomas which were individually extracted with 3 M KCl. Serial concentrations of extracts containing crude breast cancer antigens were incubated with 125I CEA and anti-CEA to obtain inhibition curves of the binding capacity. Protein concentrations were adjusted to 250 ug/0.1 ml. A curve was constructed in which the av percent binding capacity inhibition was plotted against protein concentration of the crude tumor extracts (7.8, 31.2, 62.5, 125 and 250 ug). The high values of the standard deviation determined at each point of the curve indicated the lack of homogeneity in the distribution of the immunological activity of the 48 different breast carcinomas. There was observed an immunological shifting with continual gradual quantitative and/or qualitative increase from less active to more active breast carcinomas. (22 Refs)

52. CARCINOEMBRYONIC ANTIGEN IS INCREASED IN BRONCHOALVEOLAR LAVAGE FLUID OF LUNG CANCER.

Lemarie E, Lavandier M, Renoux M, Renoux G
Services de Pneumologie et d'Immunologie, C.H.U. 'Bretonneau', Tours, France
Excerpta Med Int Congr Ser; 558:244-251 1982

Comparative carcinoembryonic (CEA) levels in the blood and the supernatant of bronchoalveolar lavage (BAL) were investigated in 117 patients classified into 4 groups: Group I 15 normal volunteers (21-68 yr old, mean age 30 yr, 7 smokers), Group II 50 non-cancerous patients (19-72 yr old, mean age 48 yr, 31 smokers), Group III 40 patients (43-71 yr old, mean age 63 yr, 22 smokers) with primary bronchial cancers, and Group IV 12 patients (40-69 yr old, mean age 56 yr, 3 smokers) who presented pulmonary metastases. Vol of the recovered lavage fluid and the cellular distributions are presented. Vol of recovered BAL liquid was similar in Group I and II. Vol of BAL was lower in Group III and smallest in Group IV because of bronchial abnormalities. Blood plasma and BAL fluid from healthy controls contained less than 10 nanog (ng)/ml of CEA with the exception of one subject, a heavy smoker. Only one Group II patient had CEA plasma titer greater than 10 ng/ml. Seven BAL Group II fluids had a titer greater than 10 ng/ml. Group III patients were tested for both blood and BAL content of CEA. Only 10 patients had CEA blood level greater than 10 ng/ml confirming that CEA blood concentration is a poor diagnostic indicator of the malignancy of a pulmonary tumor. Similar findings were observed in Group IV patients: only 4/12 blood samples had a CEA level above 10 ng/ml. In contrast, 58% of the BAL fluids from cancer-bearing patients Group III and IV had a high CEA level ranging from 17-75 ng/ml. Data indicated that a comparison between cell morphology and the CEA level is a prerequisite for interpreting the diagnostic value of increased amounts of the antigen in biological fluids. CEA level was slightly higher in smokers in both blood and BAL fluid, but the difference was not significant. (17 Refs)

53. CARCINOEMBRYONIC ANTIGEN (CEA) DETECTION IN LUNG CARCINOMA IN GREECE.

Simos A, Kotsovoulou V, Papamichail C, Kontonasiou E, Apostolopoulou P, Toubis M, Anagnostides C, Assikis J, Coutoulides C

Chest Hosp., Athens, Greece

Excerpta Med Int Congr Ser; 558:237-243 1982

Role of carcinoembryonic antigen (CEA) assays in the clinical management, diagnosis, and therapeutic monitoring of lung carcinoma (LC) was studied in 83 patients (69 males, 14 females, av age 68.4 yr) with LC, and the relationship between plasma CEA levels and the stage of tumor spread and its degree of structural differentiation was examined. Seventy patients were heavy smokers. Controls included 17 patients with pulmonary obstructive disease and pulmonary tuberculosis. Histological classification of LC patients included: 39 squamous-cell, 26 adeno-, 13 small-cell, 3 undifferentiated, and 1 large-cell carcinoma. Serum CEA levels were 50 nanog (ng)/ml or greater in 25 patients, in 58 patients levels were less than 50 ng/ml. No clear association between CEA levels and the histological type of carcinoma was observed. Among 33 patients who presented as pleurisy of unknown origin, the 16 with LC included: 6 squamous-cell, 4 adeno-, 3 small-cell, and 3 undifferentiated carcinoma. In 13 out of these 16 LC patients, CEA levels in pleural fluid were found to be greater than the corresponding serum CEA levels. In 12/16 patients CEA levels were 50 ng/ml or greater. In two patients the serum CEA levels were within normal limits although the pleural fluid levels were 50 ng/ml or greater. All 17 controls had CEA levels below 10 ng/ml in both the serum and pleural fluid. Results indicated that little or no association exists between raised CEA levels and the histological type of cancer and that measurement of CEA activity in the pleural fluid of patients suffering from pleurisy of unknown origin may be a useful adjunct for the detection of malignant effusions. (10 Refs)

54. CALCITONIN AND CARCINOEMBRYONIC ANTIGEN IN POORLY DIFFERENTIATED FOLLICULAR CARCINOMA.

Calmettes C, Caillou B, Moukhtar MS, Milhaud G, Gerard-Marchant R

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Cancer; 49(11):2342-2348 1982

Previous studies have shown that certain patients suffering from poorly differentiated follicular carcinoma (PDFC) of the thyroid had high levels of calcitonin (CT) and carcinoembryonic antigen (CEA) in the plasma. In this work, both CT and CEA were localized in tissue sections obtained at operation from patients suffering from PDFC. The results confirm the hypothesis that certain cases of PDFC are in fact CT-secreting tumors and represent another type of thyroid neoplasma. Patients suffering from PDFC should be screened using both CT and CEA assays. (Author abstract) (26 Refs)

55. CHANGING CONCEPTS IN CLINICAL RESEARCH OF PRIMARY LIVER CANCER - TEN YEARS' (1970-1979) SURVEY (MEETING ABSTRACT)

Tang ZY, Yu YQ, Lin ZY, Yang BH

Liver Cancer Research Unit, Zhongshan Hospital, Shanghai First Medical College, Shanghai, China

Asian Pacific Association for the Study of the Liver and International Association for the Study of the Liver, February 7-12, 1982, Kowloon, Hong Kong. Asian Pacific Association for the Study of the Liver and International Association for the Study of the Liver 110 pp., 1982.

Many concepts in clinical research of hepatocellular carcinoma (HCC) have been changed during the past decade. Results in a ten years' (1970-1979) survey of 615 cases and comparison between materials in 1970-1974 and 1975-1979 demonstrated that: (1) As a result of mass screening by alpha fetoprotein (AFP) and advances in early diagnosis, the number of cases of subclinical HCC as well as small HCC increased, this resulted in an increasing proportion of resection in the whole series and led to a definite improvement of ultimate outcome (5-year survival increased from 2.5% to 12.3% in the whole series, 16.3% to 39.1% in resection group). (2) Adverse to the concept of relatively short disease course, HCC does have a relatively long natural course around 24 months. (3) Some new idea concerning early development of HCC was obtained. Unicentric development was observed in 68.3% of small HCC. (4) Concepts in early diagnosis have been changed to combined analysis of AFP and SGPT. (5) Instead of nuclide imaging, angiography and B scan echography provided valuable informations for localization of small HCC. (6) Some surgical principles may have to be revised. Local resection instead of lobectomy for small tumor located in right lobe and coexisted with cirrhosis provided similar long term survival and lower operative mortality. Reoperation prolonged survival further for early recurrence and solitary lung metastasis after a radical resection. (no Refs)

56. CLINICO-PATHOLOGICAL ANALYSES OF HIGH RISK FACTORS WITH HEPATIC CELL CARCINOMA IN CHRONIC LIVER DISEASES (MEETING ABSTRACT)

Ohtoh K, Ohno H, Okuyama Y, Tsubaki K, Ohkubo H, Ishizuka H, Fujita S, Kaneda H, Honda T, Karasawa T, Shikata T
Nihon University School of Medicine, Tokyo, Japan
Asian Pacific Association for the Study of the Liver and International Association for the Study of the Liver, February 7-12, 1982, Kowloon, Hong Kong. Asian Pacific Association for the Study of the Liver and International Association for the Study of the Liver 110 pp., 1982.

Until now, we have had 68 cases of hepatic cell carcinoma (HCC) which were diagnosed histologically. Fifty-six of them were accompanied with liver cirrhosis (LC). Of these patients 74% had positive HBV (hepatitis B virus) and 85% had positive AFP (alpha-fetoprotein). Of the patients of HCC without LC, very small number had both positive HBV and AFP. So, there seem to be some risk factors with HCC in chronic liver diseases. Then, in order to clarify these, patients with various chronic liver diseases who had been observed for 3 to 8 years, analyzed clinico-pathologically. Nineteen out of 120 patients with chronic hepatitis (87 active type (CAH), 33 inactive type (CIH)) had positive AFP. The percentage of AFP positive patients with CAH (21.8%) was higher than that of ones with CIH (6.1%). Of 118 patients with LC 50 had positive HBV. In patients with LC, the percentage of AFP positive ones with positive HBV (63%) was higher than that of ones with negative HBV (29%). Sixteen patients with CH and 43 with LC were followed for many years. Thirteen out of these 43 LC cases had HCC. Of 16 cases with CH 8 had positive AFP, and all the patients with positive AFP had positive HBV. Patients who had postive AFP had a tendency to have positive HBV. The AFP values at the initial examination in all the patients were less than 200ng/ml. It seems to be important in the early diagnosis of HCC to follow up patients with chronic liver diseases and HBV and AFP. It is also considered that the presence of HBV is an important factor in the occurrence of HCC. (no Refs)

57. CLINICAL SIGNIFICANCE OF SOME TUMOR MARKERS IN HEPATOCELULAR CARCINOMA (MEETING ABSTRACT)

Fujiyama S, Tanggo Y, Tashiro A, Sagara K, Sato T
The Third Department of Internal Medicine, Kumamoto University Medical School, Kumamoto, Japan
Asian Pacific Association for the Study of the Liver and International Association for the Study of the Liver, February 7-12, 1982, Kowloon, Hong Kong. Asian Pacific Association for the Study of the Liver and International Association for the Study of the Liver 110 pp., 1982.

In order to search for another reliable marker of hepatocellular carcinoma (HCC), serial determinations of serum beta2-microglobulin (beta2-m), calcitonin and 5'-NPDase-V (5'-nucleotide phosphodiesterase) were carried out and their clinical usefulness evaluated. Serum beta2-m was determined in 373 patients with various liver diseases having normal creatinine levels. Elevation of beta2-m were observed in 35 of 47 patients (74.5%) with HCC. No significant correlation was noted between beta2-m and other tumor markers (AFP (alphafetoprotein) and Ferritin). The serum beta2-m was not closely related to tumor growth or clinical evolution. It was found that concentrations of beta2-m in ascitic fluid were much higher than that in serum. Increased serum beta2-m levels were also found in patients with chronic hepatitis (36.5%), liver cirrhosis (58.3%), and metastatic liver cancer (68.0%). Therefore, measurements of serum beta2-m seem to be of limited values in the diagnosis and monitoring of HCC. HCC patients (34.1%) had serum calcitonin values of greater than 200pg/ml. Elevated calcitonin levels were also observed in patients with chronic heptitis liver cirrhosis and metastatic liver cancer. However, HCC was highly suspected when the serum calcitonin levels rose above 500pg/ml. 5'-NPDase-V was detected in 82.4% of HCC. Of the 12 cases with low levels of AFP, 8 cases showed this Band V isozymes. Therefore, the assay of 5'-NPDase-V was particularly useful in AFP negative of low-producing HCC. The 5'-NPD ase-V was also detected in 39.3% of chronic hepatitis and 56.0% of cirrhosis. In jaundiced cases, the assay should be done carefully because of non-specific positive reaction. (no Refs)

58. CLINICAL EVALUATION OF VARIANT ALKALINE PHOSPHATASE IN PATIENTS WITH HEPATOCELLULAR CARCINOMA (MEETING ABSTRACT)

Sawabu N, Nakagen M, Wakabayashi T, Ozaki K, Toya D, Kobayashi K, Hattori N
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Asian Pacific Association for the Study of the Liver and International Association for the Study of the Liver, February 7-12, 1982, Kowloon, Hong Kong. Asian Pacific Association for the Study of the Liver and International Association for the Study of the Liver 110 pp., 1982.

We attempted to evaluate the so-called variant alkaline phosphatase (VAP), one of the alkaline phosphatase (AP) isoenzyme which was discovered by Warnock in comparison with the clinical value of tumor markers such as alpha-fetoprotein (AFP), and novel gamma-GTP (gamma guanosine triphosphate) isoenzyme (novel gamma-GTP) to be specific for hepatocellular carcinoma (HCC) reported in our previous publications. Materials consisted of sera obtained from 253 patients with various hepatobiliary diseases including 94 with HCC and 65 with cancer other than HCC. Separation of VAP and novel gamma-GTP were carried out by polyacrylamide gradient gel electrophoresis. AFP was determined by specific radioimmunoassay. VAP was detectable in 17 of 94 (18.1%) patients with HCC, but not in patients with other diseases. On the other hand, 59 out of 94 patients (62.8%) with HCC showed more than 400 ng/ml of AFP, the value to be highly indicative of HCC. And the novel gamma-GTP could be found in 61.7% of the patients. Therefore, the prevalence of VAP was lower than that of AFP or novel gamma-GTP. However, the appearance of VAP had no relation to serum titer of AFP or the positivity of novel gamma-GTP, and in 4 of 94 patients with HCC, VAP was only detected among these three markers. (no Refs)

59. A COMPARISON OF TRANSCATHETER ARTERIAL EMBOLIZATION WITH ONE SHOT THERAPY FOR THE PATIENTS WITH HEPATIC CELL CARCINOMA (MEETING ABSTRACT)

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Asian Pacific Association for the Study of the Liver and International Association for the Study of the Liver, February 7-12, 1982, Kowloon, Hong Kong. Asian Pacific Association for the Study of the Liver and International Association for the Study of the Liver 110 pp., 1982.

It is confirmed gradually that the transcatheter arterial embolization is the most effective, conservative therapy for the treatment of unresectable hepatic cell carcinoma (hepatoma). Embolization or one shot therapy were carried out in clinical trial involving 41 patients with unresectable hepatoma visiting in our department. Embolization group (emboli G): 19 cases. One to 6 times embolizations in each case. One shot group (one shot G): 22 cases. Used medications: Mitomycin C 10-40 mg and others. A vascular catheter was inserted superselectively into hepatic artery branch feeding a tumor, and through the catheter gelatin sponge particles were infused. Gelatin sponge was cut into pieces of 1-2 mm in size and soaked with anticancer drug and a contrast media (76% urografin). Disappearance rate of icterus after treatment was 50% (emboli G) and 25% (one shot G). Decrease in size of hepatomegaly or tumor were seen in 84% (emboli G) and 32% (one shot G) which was statistically significant. Serum AFP (alpha fetoprotein) titer after embolization was decreased in all of cases but 5 of 12 cases in one shot G. Effective cases measured by Karnofsky's method were 18 out of 19 cases in emboli G, but in one shot G only 10 out of 22 cases. Survival rate after each therapy showed 67% (emboli G) and 38% (one shot G) in months, and 60% (embolic G) and 20% (one shot G) in 1 year respectively. (no Refs)

60. REGIONAL INTRAARTERIAL INFUSION OF CISPLATIN IN PRIMARY LIVER CANCER: A PHASE II TRIAL (MEETING ABSTRACT)

Cheng E, Watson RC, Fortner J, Kemeny N, Golbey R
Memorial Sloan-Kettering Cancer Center, New York, NY, 10021
Proc Am Soc Clin Oncol; 1:C-695 1982

Therapeutic evaluation of intraarterial infusion has been carried out in 16 patients (pts) with primary liver cancer. Pt characteristics included: median age 50 yrs, median performance status 70%. Prior therapy included: none in 13, the other three received various combinations of Adriamycin, 5 FU (5-fluorouracil), Actinomycin D, Methotrexate, Cytoxan and M-AMSA (amsacrine). Measurable disease included: hepatomegaly and positive scan in 16, lung lesions in 3, pelvic mass in 1, elevated alpha-fetoprotein (AF) in 9. Temporary placement (femoral approach) of the catheter in the hepatic artery (ha) was performed in all but 3 who had permanent ones in place in the ha. All pts had a creatinine clearance of greater than 60 ml/min. After overnight prehydration, Cisplatin 120 mg/m2 was infused intraarterially over 2 hours with the usual mannitol diuresis and fluid support. There were no catheter complications. Nausea and vomiting was universal. Other toxicities included: wbc less than 3000/mm3 (3) and a platelet count less than 100,000/mm3 (3), reversible renal dysfunction (7), and dose-limiting paresthesia (2). If progression of disease was noted after one dose or if no response was noted after 2-3 doses, the treatment was discontinued. Mean number of doses was 2.7 (range 1-9), and mean total dose was 518 mg (210-1800). Responses were noted in 3/15 (20%) evaluable pts for 1+, 8+, and 10+ months. One pt had 75% decrease in tumor size and a decrease in AFP from 1,000,000 to 3,000 units lasting 10+ months. (no Refs)

61. CISPLATIN (DDP), AN EFFECTIVE THERAPY FOR UNRESECTABLE OR RECURRENT HEPATOBLASTOMA (MEETING ABSTRACT)

Champion J, Green AA, Pratt CB
St. Jude Children's Research Hospital, Memphis, TN, 38101
Proc Am Soc Clin Oncol; 1:C-671 1982

Unresectable or recurrent hepatoblastoma (URHB) is almost always fatal with a median survival of 6 months. Of 11 children seen at St. Jude from 1964 to 1979 with URHB 10 died 0.5 to 17 months (median 8 mos) after onset of unresectability. One patient responded to radiation and vincristine sufficiently to allow total resection of tumor. Vincristine (VCR) and 5-FU (5-fluorouracil) had provided the best clinical response with 3 of 9 patients achieving a partial response. Since 1979, 5 additional patients with URHB resistant to VCR, 5-FU, adriamycin and cyclophosphamide received DDP 90 mg/m2 q 3 weeks. All patients had intrahepatic abdominal tumor and 2 had pulmonary involvement. Clinical response was noted in 4 with 1 CR (complete response), 2 PR (partial response), and 1 mixed response (MR). All lung metastases have cleared but to date only 1 patient had complete regression of abdominal tumor. From 3 to 6 courses of DDP have been given with maximal tumor regression observed by the 4th course. One child had progressive disease after 3 courses of DDP. The child achieving MR had no recurrence of pulmonary disease at death 4 months after cessation of therapy. The overall survival time from tumor recurrence or unresectability for these 5 children is 6+, 9, 13+, 14 and 24+ months. Alpha fetoprotein (AFP) serum concentrations were reduced 1000 fold in responders although none returned to normal. Despite extensive disease and prior therapy, all patients tolerated DDP well. Transfusion was required by 2 patients and elevated BUN (blood-urea nitrogen) and creatinine was noted in 2 patients. Tumor response to DDP has increased the survival of previously unresponsive patients. Three patients were rendered tumor free, 2 with additional surgery after partial responses to DDP. (no Refs)

62. CLINICAL STUDIES WITH A NEW CANCER-ASSOCIATED ANTIGEN, CSAP (MEETING ABSTRACT)

Shochat D, Pant KD, Nelson MO, Goldenberg DM
University of Kentucky Medical Center, Lexington, KY, 40536
Fed Proc; 41(3):727 1982

Colon-specific antigen-p (CSAp) is a recently described oncofetal antigen that is quantitatively increased in colorectal and pancreatic neoplasms. It is restricted primarily to gastrointestinal tissues, but is present also in some ovarian mucinous adenocarcinomas. The results of testing for CSAp in the blood of 272 subjects with diverse diseases by a radiometric immunoassay has revealed elevations in 61% of colorectal cancer, 18% of non-neoplastic benign gastrointestinal disorders, 20% of gastric cancer, 20% of pancreatic cancers, 5% of breast cancers, 0% of ovarian cancers, and 3% of normal individuals. In combination with the CEA (carcinoembryonic antigen) test, the CSAp assay appears to increase the former's specificity for colorectal cancer. Gel diffusion studies indicated that the CSAp's in the plasma and tumors of colorectal and pancreatic cancer patients are immunologically identical. Initial clinical studies involving the injection of radioactive (131-I) goat antibodies to CSAp have shown that colorectal cancer metastases could be localized by external scintigraphy. Thus, CSAp appears to have a potential role in cancer immunodiagnosis and radioimmunodetection, particularly for colorectal and pancreatic carcinomas. (no Refs)

63. MITOCOF (MITOMYCIN, CCNU, VINCRISTINE, 5-FLUOROURACIL) IN THE MANAGEMENT OF ADVANCED COLORECTAL CANCER (MEETING ABSTRACT)

Polackwich RJ, Bullock P, Peters-Dudney BJ, Radice PA
Tampa Bay Oncology Group, Tampa, FL, 33614
Proc Am Soc Clin Oncol; 1:C-390 1982

Twenty-five patients with metastatic colorectal cancer were managed with combination chemotherapy (MitoCOF) on the following dose schedule: Mitomycin C 8 mg/M2 day 1, CCNU (lomustine) 50 mg/M2 day 1, Vincristine 1.4 mg/M2 day 1, 5-fluorouracil 300mg/M2 days 1-5. The cycle was repeated every 4-5 weeks. All patients had metastatic symptomatic disease and some patients had been followed with asymptomatic metastases for up to 2 years before beginning on treatment. Most patients had Karnofsky Performance Scores of 30-60% at the time treatment was instituted. Six patients had received prior chemotherapy with alternative 5-fluorouracil regimens. Twenty of 25 patients are currently evaluable (3 patients on study less than 2 months and 2 early deaths). Twenty of 20 evaluable patients had pre-treatment evaluation of CEA (carcinoembryonic antigen) with a mean of 612 ng/ml. Repeat CEA's performed 30-90 days after initiating MitoCOF revealed a mean CEA of 309 ng/ml with 14/20 patients experiencing a reduction in CEA levels. Seventeen of 20 patients had concomitant palpable masses, abnormal liver scans, or chest x-rays with 11/17 experiencing stable or improving disease after 90 days. The 6 patients with progressive elevations of CEA also had progressive deterioration of x-ray or scans. Cumulative thrombocytopenia represented the primary hematologic toxicity. The median duration of survival is 177+ days (range 60-320 days). (no Refs)

64. SERIAL CARCINOEMBRYONIC ANTIGEN (CEA) IN METASTATIC BREAST CANCER (MBC) (MEETING ABSTRACT)

Mughal A, Hortobagyi G, Fritsche H, Buzdar A, Yap H, Blumenschein G, Swanson D
M. D. Anderson Hospital and Tumor Institute, Houston, TX, 77030
Proc Am Soc Clin Oncol; 1:C-315 1982

One hundred sixty-seven patients (pts) with MBC were treated with combination chemotherapy including 5-fluorouracil, doxorubicin and cyclophosphamide (FAC). All pts had plasma CEA determinations performed before FAC and serially thereafter. CEA levels were measured by a triple isotope, double antibody radioimmunoassay. The median follow-up was 15 months. Eighty-four pts had abnormal initial CEA values greater than 6 ng/ml (greater than 10 ng/ml for smokers). Forty-seven of 84 (56%) pts had complete response (CR)+ partial response (PR). All responding pts had gradual decrease in CEA levels. Response and remission duration (RD) were similar in patients with normal and abnormal CEA value. Nine patients had a rise in CEA level during initial 8 weeks of therapy. Repeat CEA level in 4 weeks decreased and all patients had clinical response. Pts in whom elevated pretreatment CEA levels returned to normal during therapy had longer RD (22 months) than responding pts in whom CEA did not become normal (8 months). Two consecutive CEA changes in the same direction correlated with response in 68 of 71 (95.7%) pts. Thirty-five of 38 pts who had progressive disease evidenced increasing CEA levels. Serial CEA level provided a lead time of 1 to 13 months (median 3 months) before clinical relapse was detected in 63% of pts. Two consecutive rising CEA values correlated with progression in 91.4% of pts. CEA is a useful marker for monitoring the clinical course of MBC. Early false rise in CEA level may occur with chemotherapy. Its use for early detection of progressive disease or as an additional criterion of response to systemic therapy makes it a valuable biologic marker. (no Refs)

65. CEA IN OVARIAN CANCER (MEETING ABSTRACT)

Malkin A, Kellen JA, Malkin DG, Sturgeon JF, Dembo AJ, Reid JG, McCabe EM
Sunnybrook Medical Centre, Toronto, M4N 3M5, Canada
Proc Am Soc Clin Oncol; 1:C-30 1982

The prognostic value of sequential carcinoembryonic antigen (CEA) tests was evaluated in 325 patients with ovarian cancer participating in a clinical trial. The initial CEA was determined within one to three months following surgery and at least four tests extending over six months were performed serially on all patients. We had established previously that CEA estimations are prognostic of survival independent of stage. In the present study, we tried to determine whether sequential CEA estimations are prognostic of recurrence and survival independent of the classical prognostic factors - stage, histopathologic differentiation and amount of residual disease following surgery. The sequential estimations were categorized as to whether the CEA levels were persistently abnormal, normal, rising, falling or variable. Using a log rank analysis, we found that sequential CEA estimations per se are prognostic of recurrence and survival and, when corrected for stage, tumor differentiation and residual disease following surgery remained prognostic of both recurrence and survival. Whether the persistent elevation of CEA reflects the presence of residual disease undetectable by other means or identifies a particularly malignant phenotype remains to be determined. (no Refs)

66. URACHAL CARCINOMA AND CARCINO-EMBRYONIC ANTIGEN (MEETING ABSTRACT)

Stein BS, Goldstein I
No affiliation given
77th Annual Meeting of the American Urological Association, Inc., May 16-20, 1982, Kansas City, Missouri. American Urological Association 254 pp., 1982.

Four tissues specimens from three cases of urachal adenocarcinoma were examined for tissue levels of carcino-embryonic antigen (CEA). In two cases the lesin was localized, and subsequent serum CEA levels have remained normal. In one patient the CEA level, initially within normal limits, rose precipitously and was associated with locally recurrent tumor. All 4 specimens were examined by peroxidase-antiperoxidase methods for tissue levles of CEA. In all cases the glands and any mucin produced in them stained intensely for CEA. Thus it appears that all urachal adenocarcinomas may produce CEA regardless of the levels measured in the serum. SErum levels may be helpful as a serum tumor marker post-operatively, to indicate recurrent disease. (no Refs)

67. THE TIMING OF CYTOREDUCTIVE SURGERY (CSURG) IN MEN WITH GERM CELL TUMORS (GCT) (MEETING ABSTRACT)

Lange PH, Vogelzang NJ, Anderson RW, Fraley EE, Allen DW
Department of Urologic Surgery, University of Minnesota, Minneapolis, MN, 55455
Proc Am Soc Clin Oncol; 1:C-267 1982

It is known that Cisplatin-based chemotherapy (CT) coupled where appropriate with CSurg is effective in GCT. Yet when carcinoma (Carc) rather than only necrosis/fibrosis (N/F) or teratoma (T) is found at CSurg, the prognosis is poor. We reported apparent accelerated growth after CSurg in 8 GCT patients (pts), an event which we now call the 'take off phenomenon' (TOP) and define as rising AFP (alpha fetoprotein) and/or hCG (human chorionic gonadotrophin) levels within 30 days after CSurg. Since our report we performed 24 CSurg's in 16 pts (av follow-up 19.3 mos). Histology was N/F (9), Carc (11), T (4). After 7 CSurg's in 5 pts (2 N/F, 4 Carc, 1 T) TOP occurred: in the 6 that were closely monitored, AFP/hCG began rising 10.3 days after CSurg and in all 7, disease developed within 60 days -4 of these 5 pts never again became CR (complete response) and died. However, after 17 CSurg's in 11 pts (7 N/F, 7 Carc, 3 T) TOP did not occur and their disease remained stable for 6 mos - in 10 of these 11 pts, continuous

CR has been achieved. All 7 CSurg's with TOP had rising AFP/hCG levels before CSurg, although in 6 pts levels were normal 2 mos before and in 5 pts levels were normal at the time CSurg was planned. Conversely before surgery all CSurg's without TOP had normal AFP/hCG levels (15), normalizing values (1), or an elevated AFP secondary to liver dysfunction (1). (no Refs)

68. AN APPROACH TO THE TREATMENT OF PATIENTS WITH HEPATOCELLULAR CARCINOMA WITH PURIFIED HORSE ANTIBODY TO HUMAN ALPHA-FETOPROTEIN WITH SPECIAL REFERENCE TO THE SUPPRESSION OF SERUM AFP LEVEL (MEETING ABSTRACT)

Koji T, Munehisa T, Ishii N, Kusumoto M, Kaneda H, Ishizuka H, Taga H, Suzuki Y, Hirai H, Tsukada Y, Hara A
Department of Internal Medicine, Nagasaki University Hospital, Nagasaki, Japan
Asian Pacific Association for the Study of the Liver and International Association for the Study of the Liver, February 7-12, 1982, Kowloon, Hong Kong. Asian Pacific Association for the Study of the Liver and International Association for the Study of the Liver 110 pp., 1982.

It has ben demonstrated that the horse antiserum to rat alpha-fetoprotein (AFP) is cytotoxic and inhibits the growth of rat hepatoma cells which produce AFP. Ten patients with advanced hepatoma associated with cirrhosis were given with the antibody and changes in serum AFP levels and clinical course were observed. Horses were immunized with human AFP and the antibody was purified with an immunoadsorbent column. One mg of the purified antibody bound 100-150 ug of AFP. Dosage of the antibody given were 100-450 mg per patient depending on their AFP levels. The antibody was slowly dripped iv with saline. In all cases the serum AFP level decreased rapidly to 0 level but increased again after 1-2 weeks. However in 2 cases, the decreased low level was maintained for long periods of 10 and 24 weeks, respectively. Since the antibody administered are cleared from serum within 1 week, it was considered that such maintenance of a low level is caused by the antibody directly suppressing the production of AFP in the tumor cells. In the 1 case which maintained low AFP level over an extended period, there was a temporary improvement of clinical findings. There were no notable side effect except complications of slight serum sickness in 2 cases only. (no Refs)

69. INVESTIGATION OF A VINDESINE-ANTI-CARCINOEMBRYONIC ANTIGEN (CEA) CONJUGATE IN VIVO IN MAN (MEETING ABSTRACT)

Ford CH, Newman CE, Johnson JR, Woodhouse CS, Reeder TA, Rowland GF, Simmonds RA
Oncology Research Laboratories, Memorial University and Newfoundland, Cancer Treatment and Research Foundation Newfoundland, Canada
Proc Am Soc Clin Oncol; 1:C-148 1982

A vindesine-anti-CEA conjugate known to be cytotoxic for a cultured lung cancer cell line which expresses CEA was administered to 8 patients with advanced metastatic adenocarcinomas to determine whether (1) 131I labelled conjugate would localize in vivo (2) an escalating dose of conjugate could be safely administered. An aliquot of each batch of conjugate was iodinated with 131I and between 230-520 ug of immunoglobulin (Ig) associated with 6-14 ug vindesine (Vds) and 541-1014 uCi of radioactivity was administered to 3 pairs of patients, 4 with ovarian and 2 with colorectal primaries. Five out of 6 showed convincing localization using subtraction scanning techniques, the sixth was equivocal. The first pair subsequently received 1.2-1.5 mg Ig conjugated to 24-30 ug Vds; the second pair 11 mg Ig conjugated to 300 ug Vds and third pair 33 mg Ig conjugated to 700 ug Vds. Because of aggregation of the 4th batch of conjugate the last pair received conjugate first, and were then scanned with unconjugated radiolabelled antibody. It is estimated they received 21-42 mg Ig conjugated to 900-1800 ug Vds. All conjugates retained anti-CEA activity after conjugation when measured in an enzyme-linked immunosorbent assay and no overt toxicity was encountered. We conclude that this conjugate can be safely administered to patients and further characterization of such conjugates, including monoclonal antibody conjugates, are in progress. (2 Refs)

70. DAUNOMYCIN TARGETING TO HUMAN COLON CARCINOMA CELLS USING MONOCLONAL ANTIBODIES (MEETING ABSTRACT)

Page M, Emond JP, Dumas L
Department of Biochemistry, Faculty of Medicine, Universite Laval, Quebec G1K 7P4, Canada
Proc Am Assoc Cancer Res; 23:817 1982

A new approach to chemotherapy using monoclonal antibodies for drug targeting to the tumor cell is reported. Daunomycin was covalently bound to monoclonal antibodies directed against carcinoembyronic antigen (CEA) with 0.01% glutaraldehyde in various drug:protein ratios. The pharmacological activity of the drug-antibody conjugate was assayed in vitro with human adenocarcinoma cells producing CEA. Using a semiautomatic procedure for counting cell growth and inhibition of colony formation a minimum contact period of 10 minutes was required for full pharmacological activity of the drug-antibody conjugate. We found no significant difference in the activity of the antibody alone as compared to the control. At 500 ng/ml however, the activity of antibody bound daunomycin was 800% the activity of an equivalent amount of free daunomycin; the activity of free antibody was only 2.2% while the physical addition of both antibody and daunomycin gave 116% of the activity of the free drug alone. This new approach offers a potential application in cancer treatment since the drug carrier is directed against an already cancer marker. (no Refs)

71. MURINE MONOCLONAL ANTIBODY INFUSIONS IN CANCER (MEETING ABSTRACT)

Dillman RO, Royston I
University of California San Diego School of Medicine, La Jolla, CA, 92093
Fed Proc; 41(3):363 1982

We have infused 1 to 50 mg of anti-T cell, anti-CEA, and anti-melanoma murine monoclonal antibodies (MoAbs) into cancer patients with advanced, refractory chronic lymphocytic leukemia, lymphoma, cutaneous T-Cell lymphoma (CTCL), colorectal carcinoma and melanoma. Rapid infusions of MoAbs were occasionally associated with systemic reactions including hypotension and dyspnea. Slower infusions were without complication. Tumor-associated-antigen positive cells were rapidly cleared by such therapy, but the effect was relatively brief. MoAb binding to the relevant circulating cells was demonstrable, but uptake into solid tumor masses has not yet been seen. Studies with radiolabeled autologous leukemia cells suggested that circulating cells which bound MoAb were cleared in the reticuloendothelial system. A patient with CTCL had a prompt improvement in erythroderma in addition to a decrease in Sezary cells. To date we have not encountered problems with endogenous anti-mouse antibodies, antigenic modulation, or immune complex disease. At present we are studying the effect of a frequent schedule of MoAb administration. These agents have great potential for use alone or conjugated to immunotoxins, radioisotopes, or chemotherapeutic agents. Preliminary trials such as ours will provide a basis for rational use of such preparations in carefully designed, prospective trials for anticancer efficacy. (no Refs)

72. NEUTRON-CAPTURE THERAPY OF HUMAN CANCER: IN VITRO RESULTS ON THE PREPARATION OF BORON-LABELED ANTIBODIES TO CARCINOEMBRYONIC ANTIGEN.

Mizusawa E, Dahlman HL, Bennett SJ, Goldenberg DM, Hawthorne MF
Dept. Chemistry, Univ. California at Los Angeles, Los Angeles, CA, 90024
Proc Natl Acad Sci USA; 79(9):3011-3014 1982

Two samples of 2-phenyl-1,2-dicarba-closo-[1-3H]dodecaborane(12) were prepared by treating 1-lithio-2-phenyl-1,2-dicarba-closo-dodecaborane(12) with 3H2O (0.1 and 5.0 Ci/ml, respectively). These tritiated phenylcarborane samples were subsequently converted to corresponding samples of p-[1,2-dicarba-closo-[3H]dodecaboran(12)-2 yl]benzenediazonium ion ([3H]DBD) suitable for azo-coupling reactions. Reaction of the two tritiated diazonium ion samples with 2-naphthol resulted in the formation of an azo dye (epsilon = 1.98 x 10(4) M-1 cm-1 at 485 nm). Experiments relating absorbance to 3H activity proved the two [3H]DBD sources to have 3.81 x 10(11) and 2.45 x 10(13) cpm of 3H per mol of tritiated carborane substituent. Purified antibodies to carcinoembryonic antigen were coupled to the [3H]DBD and, after extensive dialysis, the average number of carborane moieties per antibody molecule was determined by measuring the 3H activity associated with a known protein concentration. Further examination of these tritiated carborane-labeled antibodies by affinity chromatography proved that boron labeling did not destroy their immunoreactivity. Correlations of azo-coupling conditions (reactant ratios, pH) with immunoreactivity and antibody protein recovery are presented. (Author abstract) (20 Refs)

73. LOCALIZATION OF CARCINOMAS BY PHOTOSCANNING AND TOMOSCINTIGRAPHY AFTER INJECTION OF RADIOLABELLED MONOCLONAL ANTI-CEA ANTIBODIES (MEETING ABSTRACT)

Mach JP, Buchegger F, Berche C, Lumbroso JC, Forni M, Ritschard J, Haskell C, Girardet C, Schreyer M, Accolla R, Carrel S
Ludwig Institute for Cancer Research, Lausanne, Switzerland
Hybridoma; 1(2):186 1982

Monoclonal antibodies (Mabs) against specific epitopes of carcinoembryonic antigen (CEA), labeled with 131I and normal mouse IgG (polyclonal or monoclonal), labeled with 125I were injected into nude mice bearing grafts of human colon carcinoma and in patients with large bowel, pancreas or medullary thyroid carcinomas. In nude mice the tumor uptake as compared to all normal tissues ranged from 7 to 15 fold greater for Mabs and 1-4 for normal IgG, resulting in specificity indices ranging from 4-6. In patients, the tumors resected after injection showed a Mabs uptake ranging from 2 to 10 and specificity indices ranging from 2-7. Detection of 131I Mabs by standard photoscanning, helped by computerized subtraction of 99mTc labeled albumin, allowed the localization of 14 carcinoma in 28 patients. Detection of the same labeled Mabs by single photon emission computerized tomography (SPECT) allowed the localization of 16 tumor sites out of 17 studied in 17 other patients. The results indicate that the use of the most modern tool of immunology (Mabs) and of nuclear medicine (SPECT) improves the specificity and sensitivity of immunoscintigraphy. Furthermore, we think that such detections and the paired labeling experiments described, should be performed in nude mice and in patients with each new Mabs against solid tumors which are seriously considered for various forms of passive immunotherapy. Although no side effects were observed, we consider that these injections in patients should be restricted to strictly controlled scientific studies. (1 Ref)

74. RADIOIMMUNODETECTION OF HEPATOCELLULAR CARCINOMA WITH RADIOLABELED ANTIBODIES TO ALPHA-FETOPROTEIN (MEETING ABSTRACT)

Ishi N, Nakata K, Muro T, Kono K, Furukawa R, Kusumoto Y, Munehisa T, Koji T, Nagataki S, Hirai H
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Asian Pacific Association for the Study of the Liver and International Association for the Study of the Liver, February 7-12, 1982, Kowloon Hong Kong. Asian Pacific Association for the Study of the Liver and International Association for the Study of the Liver 110 pp., 1982.

The present study was undertaken to investigate whether radiolabeled anti-alpha-fetoprotein (AFP) antibody administered intravenously can be accumulated in AFP-producing tumors. Rats with subcutaneously transplanted hepatoma and with intrahepatic tumor produced by 3'-Me-DAB (3'-methyl-4'-diaminoazobenzene) feeding, and 11 patients with hepatocellular carcinoma (HCC) were studied. In animal experiments, the tumor localization of radioiodinated horse antibody to AFP was demonstrated 48 to 168 hours after the injection by total body scintigraphy and radioactivity in the tumors was the highest among organs counted after sacrifice. In patients with HCC, images were made with a gamma camera usually at 24 and 48 hours after injection of 0.8 to 1.7 mCi of I-131-labeled horse anti-human AFP antibody. In order to reduce background, nonspecific radioactivity, subtraction of images derived from Tc-99m-labeled serum albumin and technetium pertechnetate from the I-131 scans is accomplished with a computer. In 6 of 11 patients with HCC, the tumor location could be demonstrated on this method. However, tumors below 2 cm in diameter which were detected by the celiac angiography were not detectable. It is interesting that we could get positive scanning in 5 cases even though their serum AFP levels were very high. The chromatographic profiles of serum after the injection of the radioantibody to AFP showed two peaks of radioactivity, suggesting the immune complex and the free antibody to AFP. No remarkable side effects were observed. (no Refs)

75. A CORRELATIVE STUDY OF CARCINOEMBRYONIC ANTIGEN (CEA) RADIOIMMUNODETECTION (RAID) IN THE EVALUATION OF HEPATIC METASTASES (MEETING ABSTRACT)

Goldenberg DM, Kim EE, Bennett SJ, Shah U, Nelson MO, DeLand FH
University of Kentucky Medical Center, Lexington, KY, 40536
Proc Am Soc Clin Oncol; 1:C-391 1982

Twenty-nine patients with histologically-confirmed liver metastases from diverse cancer types were evaluated retrospectively by liver function tests, such as SGOT and Alk Pase, plasma CEA, colloid scans of the liver (RN), ultrasonography (US) in 14 patients, computed tomography (CT) in 8, and by CEA-RAID. In the RAID studies, the patients received iv infusions of 1-2.5 mCi of 131-I-labeled CEA antibody IgG containing about 250 ug of antibody protein. Images of the chest and abdomen were made usually at 24 and 48 hrs, and nonspecific background activities were removed by computer-assisted subtraction of 99m-Tc images. CEA-RAID was capable of revealing cancers in the liver in 97% of the cases; circulating CEA did not appear to affect the success of tumor RAID. CT scans were positive in 75% of the small series of 8, while US had a 79% sensitivity in 14 patients. Liver RN scans showed 20 of 27, or 85%, true-positives. Thus, CEA-RAID was able to complement these other methods used to disclose liver metastases. In terms of liver function and CEA tests, SGOT was elevated in 59% of the cases, Alk Pase in 69% and CEA in 72-93%, depending upon the cutoff. CEA-RAID was consistently positive in patients with CEA titers below 10 ng/ml (8/29). CEA-RAID can reveal hepatic metastases even when other modalities, such as liver colloid scans, are negative or equivocal, and also appears to be a more sensitive indicator of liver involvement than the plasma CEA test. (no Refs)

76. CARCINOEMBRYONIC ANTIGEN (CEA) RADIOACTIVE ANTIBODY FRAGMENTS FOR CANCER LOCALIZATION IN VIVO (MEETING ABSTRACT)

Gaffar SA, Bennett SJ, DeLand FH, Primus FJ, Goldenberg DM
University of Kentucky Medical Center, Lexington, KY, 40536
Proc Am Assoc Cancer Res; 23:965 1982

Previous experimental and clinical studies have indicated that radioactive antibodies to CEA can be used for the in vivo, external detection of CEA-producing tumors by the method of radioimmunodetection. These experiments involved the administration of affinity-purified, whole IgG goat antibody. In order to achieve a more rapid tumor accretion by a less immunogenic diagnostic reagent, the efficacy of F(ab')2 and Fab' fragments of the CEA antibody IgG were compared to that of whole antibody IgG and to normal goat IgG fragments. Tumor radiolocalization was evaluated in the GW-39 human colonic carcinoma growing in hamsters and producing CEA. In terms of antibody activity, the animals received concentrations of antibody fragments which were approximately equal to that of the intact antibody IgG, although a 50% reduction of CEA immunoreactivity was experienced in the preparation of Fab'. Tissue localization experiments (cpm/g) were performed at 1-14 hrs and 1-5 days after injection of the radioactive antibody preparations. Tumor localization (tumor/nontumor ratio) was higher for the native IgG antibody than for the antibody fragments or similar normal IgG preparations. The percentage of dose injected that was subsequently recovered in the tumor was 5-10 times higher for whole IgG antibody than for Fab', while the results for F(ab')2 were intermediate. These results suggest that whole IgG and F(ab')2 antibodies are the preferred preparations for tumor radioimmunodetection. (1 Ref)

ULTRASTRUCTURE/ CYTOCHEMISTRY

77. TISSUE DEMONSTRATION OF CARCINOEMBRYONIC ANTIGEN (CEA) IN COLUMNAR ESOPHAGEAL EPITHELIUM.

Geboes K, Vanstapel MJ, Desmet VJ, Vantrappen G
Laboratorium voor Histochemie en Cytochemie, Academisch Ziekenhuis Sint Rafael, Minderbroedersstraat 12, B-3000 Leuven, Belgium
Hepatogastroenterol; 28(6):324-326 1981

Carcinoembryonic antigen (CEA) was detected by an indirect immunofluorescence technique in biopsies of 11 patients out of a series of 23 with a lower esophagus lined by columnar epithelium. CEA-specific staining was seen in simple columnar cells and in intestinal type epithelium. The positive staining was seen as a linear luminosity along the luminal aspect of the cells. Tissue localization of CEA might help detect premalignant changes in Barrett's epithelium. (Author abstract) (12 Refs)

78. IMMUNOHISTOCHEMICAL EVALUATION OF CARCINOEMBRYONIC ANTIGEN, SECRETORY COMPONENT, AND EPITHELIAL IGA IN TUBULAR AND VILLOUS LARGE-BOWEL ADENOMAS WITH DIFFERENT GRADES OF DYSPLASIA.

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Histochemical Lab., Inst. Pathology, Rikshospitalet, Oslo 1, Norway
Scand J Gastroenterol; 17(3):341-348 1982

In a material of 513 consecutively collected large-bowel polyps, tubular and villous adenomas with corresponding histologic grades of epithelial dysplasia were selected. Fifty-two samples of the former and 27 of the latter category were evaluated semiquantitatively for immunohistochemical staining of the epithelial marker proteins carcinoembryonic antigen (CEA), secretory component (SC), and IgA. No consistent differences in the overall staining properties were found between the two types of tumors. In both categories the staining intensity for SC and epithelial IgA decreased with increasing degree of dysplasia, most strikingly so for IgA. This observation shows that the malignant alterations impair the capacity of the columnar epithelium to produce SC and to express it as a functional receptor mediating uptake of dimeric IgA. Thus, the absence of epithelial IgA in large-bowel adenomas may be a useful adjunct in grading of dysplasia. Conversely, the presence of CEA did not seem to be related to dysplastic alterations in the epithelium. (Author abstract) (35 Refs)

79. IMMUNOELECTRON MICROSCOPIC STUDY ON ALPHAFETOPROTEIN SYNTHESIS.

Lin Chu M, Chang TW, Chuong CM, Lin WS
Dept. Pathology, Coll. Medicine, Natl. Taiwan Univ., Taipei, Taiwan
Taiwan I Hsueh Hui Tsa Chih; 81(2):127-134 1982

Human fetal liver and hepatoma cells were compared with respect to ultrastructural localization of alphafetoprotein (AFP) by immunoelectron microscopy. The AFP-synthesizing cell was found to be a hepatocellular carcinoma cell with the same pattern of positive distribution of immunoenzyme reaction products characteristic of AFP in the cytoplasm as those of the fetal hepatocytes. Synthesis of AFP in the tumor state appears to be the result of depression of the oncodevelopmental protein (AFP), which after depression follows the same pathway as in the fetal state. (22 Refs)

80. DEMONSTRATION OF CARCINOEMBRYONIC ANTIGEN (CEA) BY MEANS OF THE IMMUNOPEROXIDASE TECHNIQUE IN PARAFFIN-EMBEDDED SPECIMENS OF TUMOUR TISSUES.

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Institut fur Pathologie, Medizinische Akademie Carl Gustav Carus, Fetscherstrabe 74, DDR-8019 Dresden, W. Germany
Exp Pathol; 21(2):79-88 1982

The unlabeled antibody-enzyme method with the peroxidase-antiperoxidase complex (PAP-complex) was used to demonstrate carcinoembryonic antigen (CEA) or CEA-like substances in paraffin-embedded specimens of tumor tissues with an anti-CEA-antiserum of a rabbit. The anti-CEA-antiserum used in this study exhibited a high anti-CEA-activity and a low activity to an impurity. The paraffin-embedded specimens of tumor tissues were investigated at serum dilutions of 1:16, 1:64, and 1:256. The sections of colorectal cancer showed the highest content of CEA. In 36 of 37 cases the tumor tissue reacted to the anti-CEA-antiserum up to a dilution of 1:256. The stomach cancer tissues contained significantly lower CEA-levels than the colorectal cancer. The sarcomas, malignant melanomas, the tumor of testis, the prostatic cancers and basal cell carcinoma of the skin were found to contain none or very low CEA-content. In most specimens of these tumors the CEA was not demonstrable at a 1:16 dilution of the primary antiserum. (Author abstract) (49 Refs)

81. IMMUNOHISTOCHEMICAL STUDY OF HUMAN CHORIONIC GONADOTROPIN, ALPHA FETOPROTEIN, AND BETA15B1 PREGNANCY SPECIFIC GLYCOPROTEIN IN TESTICULAR TUMOR TISSUE.

Shimatani N, Arakawa S, Masuda M, Kamidono S
Dept. Urology, Kobe Univ. Sch. Medicine, Kobe, Japan
Nippon Hinyokika Gakkai Zasshi; 72(9):1164-1176 1981

Formalin-fixed specimens of germ cell testicular tumors and tumors metastatic to retroperitoneal lymph nodes from 48 patients (8 mo-49 yr old) were examined for human chorionic gonadotropin (hCG), alpha fetoprotein (AFP), and beta1 pregnancy specific glycoprotein (SP1). Histologically, the testicular tumors included 33 pure tumors (6 adult type embryonal carcinoma, 4 infantile embryonal carcinoma, 8 teratoma, 15 seminoma) and 15 mixed tumors. Of the 25 cases of adult-type nonseminomatous germ cell tumors, sites of production of hCG, SP1, and AFP were found in 16 cases, 14, and 18, respectively. On the other hand, hCG and SP1 were not observed in 8/8 cases of infantile non-seminomatous germ cell tumors and AFP was observed in 4/8. Abnormally high levels of betahCG were observed preoperatively in 6/15 cases of seminoma; hCG and SP1 were localized in the syncytiotrophoblastic giant cells of four of the six patients. Measurement of preoperative plasma levels of betahCG and performance of immunohistochemical tests were thought to be important in diagnosing pure seminomas. (38 Refs) (In JPN)

82. ENDOCERVICAL AND ENDOMETRIAL ADENOCARCINOMA: AN IMMUNOPEROXIDASE AND HISTOCHEMICAL STUDY.

Cohen C, Shulman G, Budgeon LR
Dept. Pathology, Milton S. Hershey Medical Center, Hershey, PA, 17033
Am J Surg Pathol; 6(2):151-157 1982

A retrospective study was conducted of 13 adenocarcinomas of endocervical origin and 21 of endometrial origin with histochemical stains for type and distribution of mucin, and by carcinoembryonic antigen (CEA) immunohistochemistry. All 13 adenocarcinomas of endocervical origin contained CEA, with strongly positive immunostaining in nine. Only 11 of the 21 endometrial adenocarcinomas contained CEA. The degree of tumor differentiation was not correlated with the amount of CEA in either type of adenocarcinoma. Mucicarmine and alcian blue (AB)-positive mucin was present in 12/13 of the endocervical lesions and in 19/21 of the lesions of endometrial origin. Both poorly and moderately differentiated endocervical carcinomas contained large amounts of mucin; with endometrial carcinomas, the amount of mucin apparently correlated with tumor differentiation: better-differentiated lesions showed more mucus production than poorly-differentiated ones. Although criteria are not absolute, better differentiation of endocervical from endometrial carcinoma may be obtained by histochemical staining for the amount, distribution, and type of mucin, and the demonstration of the amount and distribution of CEA. (19 Refs)

83. CARCINOEMBRYONIC ANTIGEN AND ALPHA-LACTALBUMIN IN BREAST CARCINOMA: AN IMMUNOHISTOCHEMICAL STUDY (MEETING ABSTRACT)

Kuhajda FP, Mendelsohn G
Department of Pathology, The Johns Hopkins Medical Institutions, Baltimore, MD
71st Annual Meeting of the International Academy of Pathology (United States-Canadian Division), March 1-5, 1982, Boston, Massachusetts. International Academy of Pathology 95 pp., 1982.

Carcinoembryonic antigen (CEA) is a valuable marker in many carcinomas, whereas alpha-lactalbumin (ALA), a protein produced by breast epithelial cells, is specific for breast carcinoma. Conflicting reports exist concerning CEA and ALA in different histologic types of breast carcinoma. To evaluate the distribution and staining characteristics of these markers, we stained 62 assorted in situ and infiltrating breast carcinomas, numerous benign breast lesions, and normal breast tissue using the immunoperoxidase technique. Positive immunostaining for CEA was observed in 62 per cent of carcinomas, but not in normal breast or benign breast lesions including papillomas and duct papillomatosis. ALA was present in 76 per cent of carcinomas and focally positive in normal breast epithelium and in four papillomas. In situ lobular carcinoma stained poorly for both CEA and ALA; ALA was present in 77 per cent of infiltrating lobular carcinomas, whereas CEA was present in only 32 per cent. CEA was present in 80 per cent of intraductal and 66 per cent of infiltrating duct carcinomas; ALA was present in 80 and 84 per cent of these tumors, respectively. Lymph node metastases were more frequent in cases of infiltrating duct carcinoma with strong CEA positivity. (no Refs)

84. CARCINOEMBRYONIC ANTIGEN AND ALPHA-LACTALBUMIN IN BREAST CARCINOMA: AN IMMUNOHISTOCHEMICAL STUDY (MEETING ABSTRACT)

Kuhajda FP, Mendelsohn G
Department of Pathology, The Johns Hopkins Medical Institutions, Baltimore, MD
Lab Invest; 46(1):46A 1982

Carcinoembryonic antigen (CEA) is a valuable marker in many carcinomas, whereas alpha-lactalbumin (ALA), a protein produced by breast epithelial cells, is specific for breast carcinoma. Conflicting reports exist concerning CEA and ALA in different histologic types of breast carcinoma. To evaluate the distribution and staining characteristics of these markers, we stained 62 assorted in situ and infiltrating breast carcinomas, numerous benign breast lesions, and normal breast tissue using the immunoperoxidase technique. Positive immunostaining for CEA was observed in 62 per cent of carcinomas, but not in normal breast or benign breast lesions including papillomas and duct papillomatosis. ALA was present in 76 per cent of carcinomas and focally positive in normal breast epithelium and in four papillomas. In situ lobular carcinoma stained poorly for both CEA and ALA; ALA was present in 77 per cent of infiltrating lobular carcinomas, whereas CEA was present in only 32 per cent. There was no significant difference in CEA and

ALA staining in lymph node metastases from 14 patients. However, lymph node metastases were more frequent in cases of infiltrating duct carcinoma with strong CEA positivity. (no Refs)

85. URINARY BLADDER CYTOLOGY AND IMMUNOPEROXIDASE STAINING FOR CARCINOEMBRYONIC ANTIGEN (MEETING ABSTRACT)

Bollean MA
No affiliation given
77th Annual Meeting of the American Urological Association, Inc., May 16-20, 1982, Kansas City, Missouri. American Urological Association 254 pp., 1982.

The overall cytological accuracy for patients with histologically proven urothelial tumors is approximately 70% but varies significantly with the grade of the bladder tumor. In cases of moderately differentiated and poorly differentiated transitional cell tumors cytologies are positive in over 90% of cases. However well differentiated lesions yield negative cytology because the morphologic changes in the exfoliated cells are not sufficient to differentiate from normal cells. It has been reported that approximately 60% of well differentiated urothelial tumors have CEA (carcinoembryonic antigen)-containing cells. In an effort to increase the accuracy of cytology we have utilized immunoperoxidase staining for CEA in patients with low grade urothelial tumors. Bladder washings were obtained from 30 patients with known transitional cell carcinoma of the bladder an fixed with 50% ethanol. The cells were then placed in a cytospin centrifuge and spun on to microscope slides. An indirect immunoperoxidase labelled anti-CEA antibody technique was then used to identify urothelial cells containing CEA. A CEA-producing colon carcinoma cell line was used as a positive control. Slides from 5 patients were considered uninterpretable. Slides from 15 patients revealed urothelial cells containing CEA. Slides from the remaining 10 patients were negative. (no Refs)

86. IMMUNOCYTOCHEMICAL LOCALIZATION OF CARCINOEMBRYONIC ANTIGEN, ALPHA-FETOPROTEIN, AND HUMAN CHORIONIC GONADOTROPIN IN CERVICAL NEOPLASIA (MEETING ABSTRACT)

Bychkov V, Bardawil W, Rothman M
Department of Pathology, Abraham Lincoln School of Medicine, University of Illinois, Chicago, IL
71st Annual Meeting of the International Academy of Pathology (United States-Canadian Division), March 1-5, 1982, Boston, Massachusetts. International Academy of Pathology 95 pp., 1982.

One hundred and seven neoplastic lesions, includng 40 cases of cervical intraepithelial neoplasis (CIN), 61 cases of invasive cervical carcinomas, and six cases of vaginal and vulvar carcinomas were studied by peroxidase-immunoperoxidase method (PAP) for the presence of carcinoembryonic antigen (CEA). Forty-two cases (13 CIN and 29 invasive cervical carcinomas) were also tested for alpha-fetoprotein (AFP) and human chorionic gonadotropin (HCG). Specific antisera were obtained from commercial laboratories. Controls included absorption and neutralization of the specific antisera, substitution of specific antisera with normal sera, and inclusion in every test of known positive tissues. CEA was not detected in normal cervical epithelium but was present in 90 per cent of neoplastic lesions. Not mere presence, but the pattern of distribution of CEA emerged as the main differential point between noninvasive and invasive lesions. Twenty-nine of 51 invasive squamous cell carcinomas (57 per cent) contained CEA-positive cells at the stromal edge of epithelium, whereas this feature was never found in CIN. Adenocarcinomas and adenosquamous carcinomas (7) were all positive for CEA. All clear cell carcinomas (three) and the majority of basal cell type and poorly differentiated carcinomas were negative. AFP was present only in the case poorly differentiated 'glassy cell' carcinoma. HCG has not been revealed in any of the tumors. (no Refs)

87. DIFFERENTIAL EXPRESSION OF TUMOR ASSOCIATED ANTIGENS IN HUMAN COLON CARCINOMAS XENOTRANSPLANTED INTO NUDE MICE (MEETING ABSTRACT)

Shochat D, Gold DV, Primus FJ, Dexter DL, Calabresi P, Goldenberg DM
Department of Pathology, University of Kentucky, Lexington, KY, 40536
Proc Am Assoc Cancer Res; 23:1086 1982

Human colon carcinoma produce several organ specific and tumor associated antigens, among them CEA (carcinoembryonic antigen), CSAp (colon-specific antigen P) and CMA. We have examined the antigen profiles of a number of different human colon carcinomas xenotransplanted into nude mice, to serve as a basis for use of these tumors as models for tumor antigen purification, radioimmunodetection, immunotherapy, etc. Extreme heterogeneity in antigen expression was observed by both radioimmunoassay and immunohistochemical procedures for each antigen. Four of 10 tumors (DLD-2, 3, 5 and HCT-10) were high producers of CEA. Two of these (DLD-2 and HCT-10) correlated with high production of CSAp and CMA, while the other two produced low quantities of CSAp and CMA. Another tumor (HCT14-OMI) produced large amounts of CMA, yet moderate amounts of CEA and low quantities of CSAp. Immunohistochemical analysis of CEA gave a mostly diffuse cellular and membranous staining for all of the tumors. Staining for CSAp was very focal, as for example in DLD-5 where only a few of the tumor cells were stained. In most cases staining for CMA was limited, however, DLD-2, HCT-10 and HCT 14 OMI showed intense intracellular and intraluminal staining. The data indicates that the various tumors differ, quantitatively and qualitatively in their expression of these antigens. (no Refs)

REVIEWS/ OTHER RELATED STUDIES

88. MECHANISMS OF IMMUNITY IN CANCER.

Baldwin RW
Cancer Res. Campaign Lab., Univ. Nottingham, Nottingham NG7 2RD, England
Pathobiol Annu; 11:155-175 1981

Immunological recognition of malignant cells in human tumors, malignant melanomas, and other tumors, and the role of suppressor T cells and other suppressor factors are discussed. The tumor cell must express an appropriate tumor associated antigen for a tumor to generate specific T lymphocyte response and/or initiate antibody formation. Original evidence cited in identifying human tumor associated antigens showed that peripheral blood lymphocytes from patients were cytotoxic in vitro when tested on cultured tumor cells, reactivities indicating that many tumors exhibited tumor-type specific antigens. The reactivity of monoclonal antibody (MCAB) produced by two hybridoma lines prepared against human osteogenic sarcoma cell line is presented. Production of MCAB to melanoma associated antigens by hybridomas derived from fusion of mouse myeloma cells and spleen cells from mice immunized with cultured melanoma cells or membrane fractions was observed. The antibody preparation reacted strongly with cells of the immunizing melanoma and less strongly with an allogeneic melanoma. MCAB specifying cell surface antigens have been produced against other human tumors, including carcinomas of the colon, neuroblastoma, and leukemic cells. MCAB are being produced against a number of tumor associated substances, including carcinoembryonic antigen, human alpha-fetoprotein, and human fibrinectin. Virus related antigens upon tumor cells, such as Epstein Barr virus antigens, also can be detected by MCAB reagents. Adoptive transfer experiments also have been used to demonstrate a requirement for specifically sensitized T lymphocytes in tumor rejection. One of the most significant aspects of T lymphocyte recognition of tumor associated antigens is the finding that T suppressor cells rather than T cells mediating tumor rejection may be induced. (102 Refs)

89. BIOCHEMICAL MARKERS IN BREAST CANCER.

Coombes RC
Royal Marsden Hosp., Sutton, Surrey SM2 5PT, England
Breast Cancer Management: The Experience of the Combined Breast Clinic, St. George's Hospital/The Royal Marsden Hospital. Coombes RC, Powles TJ, Ford HT, and Gazet JC, ed. London, Academic Press, 317 pp., 1981.

The incidence of abnormal markers in localized and metastatic disease and the value of sequential marker estimations following mastectomy are discussed. Fifty-one patients admitted to a breast unit were studied for the presence of special biochemical parameters, correlation with physical staging techniques, relationship to histology, and hypercalcemia. C-reactive protein was elevated in only 2/26 patients, carcinoembryonic antigen in 3/25, ferritin in 0/25, dimethylguanosine in 2/22, and alkaline phosphatase in 0/25 patients. No difference in the marker results was observed between patients who developed metastases and those who did not. (21 Refs)

90. ON THE RELATIONSHIP OF HUMAN ONCOFETAL ANTIGEN (HOFA) TO TUMOR BURDEN IN MALIGNANT MELANOMA (MM) (MEETING ABSTRACT)

Salinas FA, Wee KH, Silver HK
Cancer Control Agency of British Columbia and University of British, Columbia British Columbia, Canada
Fed Proc; 41(3):553 1982

We have reported cross-reactivity between mouse or human extracted oncofetal antigens and human solid tumors. We now demonstrate the interaction of HOFA with selected MM patients (pts) sera using an in vitro approach. The antigen was solubilized by 3M-KCl from fetal liver tissue of non-living 19-22 wk old fetuses. HOFA is a glycoprotein containing 3% carbohydrate with pI at 5.3 and 7.0. After G-100 Sephadex purification, sucrose gradient fractionation (SGF) and polyacrylamide gel electrophoresis (PAGE) showed a single band at p15 Kilodaltons. Similar analyses on MM pts' sera reacted with 125I-HOFA showed maximal uptake by fractions larger than IgG. Immune complexes (IC) were elevated (88-258 ug/ml) in heavier fractions as compared to identically treated NCS (15-16 ug/ml). Functional characterization was performed by reacting optimal HOFA (3 ug) with selected MM pts' sera, and IC size analysis by SGF showed a significant relationship to pts' tumor burden. Based on lattice size the molecular compositions of IC were Ag2Ab1 and Ag6Ab3 for minimal tumor burden; Ag4Ab2 and Ag10Ab5 for intermedium burden and Ag4Ab2 and Ag6Ab3 for advanced disease pts' sera. Our results depict cross-reactivity between HOFA and MM pts' immune reactants, and suggest that analysis of IC size and molecular composition could help both to understand the clinical significance of IC changes and to assess pts' tumor burden. (no Refs)

91. CELL-SURFACE ANTIGENS OF A CLONAL HUMAN EMBRYONAL CARCINOMA CELL LINE: MORPHOLOGICAL AND ANTIGENIC DIFFERENTIATION IN CULTURE.

Andrews PW, Goodfellow PN, Shevinsky LH, Bronson DL, Knowles BB
Wistar Inst. Anatomy and Biology, 36th Street at Spruce, Philadelphia, PA, 19104
Int J Cancer; 29(5):523-531 1982

A cloned human embryonal carcinoma (EC) cell line has been derived from a testicular teratocarcinoma, and reproducibly forms EC tumors when injected into athymic (nu/nu) mice. These human EC cells are characterized by a newly described stage-specific embryonic antigen, SSEA-3. Unlike murine EC cells, they express major histocompatibility antigens (HLA-A, B, C and beta2-microglobulin) but do not express the embryonic antigen SSEA-1. We also report that these cells appear to be capable of differentiation and that this can be induced by initiating cultures at a low cell density. Differentiation is marked by the appearance of morphologically distinct cells and by the induction of SSEA-1, whereas the expression of other antigens, including SSEA-3, is initially diminished. This well-characterized system of human EC cells provides a model for the future investigation of other human teratocarcinoma cell lines and for the analysis of cellular differentiation during early human development. (Author abstract) (49 Refs)

92. SIMILAR GLYCOPEPTIDES IN NORMAL CHONDROBLASTS AND IN ROUS SARCOMA VIRUS-TRANSFORMED FIBROBLASTS.

Cossu G, Warren L, Boettiger D, Holtzer H, Pacifici M
(c/o Pacifici) Dept. Anatomy G3, Sch. Medicine, Univ. Pennsylvania, Philadelphia, PA, 19104
J Biol Chem; 257(8):4463-4468 1982

Fucose-labeled glycopeptides were isolated from the glycoproteins of normal chick embryo chondroblasts grown in monolayer cultures or in suspension. Analysis by chromatography on Sephadex G-50 columns revealed that a large proportion of these glycopeptides co-migrated with the large mol wt glycopeptides (Group A) reported in numerous types of tumorigenic cells. the proportion of Group A glycopeptides in normal chondroblasts was essentially identical with that found in chick embryo skin fibroblasts transformed by a temperature-sensitive mutant (ts-LA24A) of Rous sarcoma virus and grown at the permissive temperature. When chondroblasts transformed with ts-LA24A were grown at either the permissive or the nonpermissive temperature, no changes were observed in the overall pattern of glycopeptide synthesis or in the amount of Group A glycopeptides synthesized. Furthermore, when the various glycopeptides synthesized by normal and transformed chondroblasts were compared by concanavalin A-Sepharose affinity chromatography and DEAE-Sephadex ion exchange chromatography, no significant differences were found. The unusually high level of Group A glycopeptides found in monolayer or in suspension cultures of normal chondroblasts appears to be under environmental control. Thus, normal chondroblasts in vivo, as well as in organ culture, did not synthesize the large proportion of Group A glycopeptides, and the overall pattern on Sephadex G-50 column chromatography was indistinguishable from that of normal skin fibroblasts. We conclude that (1) normal chondroblasts in monolayer or suspension cultures can be induced to synthesize a class of molecules characteristic of transformed cells, and (2) though the synthesis of these glycopeptides may not be a prominent part of the normal in vivo biosynthetic program of chondroblasts, their synthesis in vitro probably reflects a response or adaptation to differences in their microenvironment. (Author abstract) (31 Refs)

93. PROTEINS AND NEOPLASTIC GROWTH.

Shapot VS
Moscow, USSR
Vestn Akad Med Nauk SSSR; (3):22-29 1982

Existence of the hypothetical tumor-specific proteins is discussed. Literature data on the tumor-associated antigens indicate that idiotypic IgM secreted by chronic lymphoid leukemia cells, transplantation antigen TL detected in the murine leukemia cells, and alpha-fetoprotein produced by hepatoma and teratocarcinoma cells are also present in the normal and embryonal tissues and that the mere presence of these proteins in the normal tissue is not associated with neoplastic transformation of these tissue. Such embryonal proteins as alpha-fetoprotein, trophoblastic protein, or carcinoembryonal antigen can be used as the diagnostic markers of the neoplastic growth. (38 Refs) (In RUS)

94. ANTIGENIC HETEROGENEITY OF AN ESTABLISHED HUMAN GLIOMA CELL LINE (HGCL) AND EIGHT SINGLE CELL DERIVED CLONES AS DEFINED BY SPECIFIC ANTI-GLIOMA MONOCLONAL ANTIBODIES (MCA) (MEETING ABSTRACT)

Wikstrand CJ, Bigner SP, Bigner DD
Duke University Medical Center, Durham, NC, 27710
Proc Am Assoc Cancer Res; 23:1070 1982

Antigen heterogeneity of the characterized established HGCL D-54 MG and eight single cell-derived clones was examined with 3 anti-D-54 MG MCA by cell surface radioimmunoassay (CS-RIA), indirect immunofluorescence (IF), and peroxidase-anti-peroxidase immunohistochemistry (PAP). D-54 MG exhibits glial morphology in vitro, is tumorigenic in nude mice, and contains 6 distinct marker chromosomes; 8 clones derived from this line indicate at least 3 separate cell subpopulations defined by morphology and reactivity with a panel of analytically absorbed non-human primate anti-glioma sera. Three MCA raised against D-54 MG exhibit restrictive reactivity patterns: all are nonreactive with adult human PBL, brain, liver, spleen, kidney, muscle, and lung; and with carcinomas (cervical, ovarian bladder, colon, and prostatic), sarcomas (osteogenic, leiomyosarcoma, and fibrosarcoma) and with melanomas by CS-RIA, IF, and PAP. One MCA detects an oncofetal determinant shared by neuroblastomas and fetal fibroblasts; two anti-D-54 MG MCA are highly restrictive, binding to 8/15 or 11/16 glioma samples respectively, while unreactive with neuroblastomas, fetal skin and thymus. Analysis of the 8 clones with anti-D-54 MCA revealed antigenic heterogeneity among the clonal subpopulations unrelated to morphologic classification; patterns of reactivity with these MCA were consistent with the assumption of a minimum of 3 distinct immunogenic, glioma-associated determinants expressed by the parent HGCL. The data establish 1) a cultured HGCL maintained antigenically distinct cell subpopulations for more than 50 passages in vitro; 2) MCA induced vs this cell line detected determinants restrictively expressed by human gliomas and/or neuroblastomas; and 3) these specificities are not related to previously described oncofetal neuroectodermal antigens. (no Refs)

95. TRIAL OF AN AROMATIC RETINOID (AR) IN PATIENTS WITH SOLID TUMOURS (MEETING ABSTRACT)

Rustin GJ, Bagshawe KD

Department of Medical Oncology, Charing Cross Hospital, London, England

Br J Cancer; 44(2):290 1981

Retinoids can inhibit growth of several experimental tumors and stimulate differentiation of mice embryonal carcinoma cells. The effect of hypervitaminosis A induced by an aromatic retinoid (RO 10-9359) was assessed in 18 patients with advanced measurable cancer. Patients received AR for a minimum of 4 weeks. Hypervitaminosis A was judged to be present when the patients exhibited signs such as chelitis, and was maintained by 25-50 mg of AR per day. All patients had received prior cytotoxic chemotherapy, and their types of tumor were metastatic testicular teratoma (6), ovarian adenocarcinoma (4), metastatic melanoma (2), bronchial adenocarcinoma (1), breast adenocarcinoma (1), colonic adenocarcinoma (1), uterine leiomyosarcoma (1), diffuse lymphocytic lymphoma (1) and Hodgkin's disease (1). There was disease progression while receiving AR in all patients except a female with lymph-node metastases from ovarian adenocarcinoma, who had a marginal response for 2+ months, and in a female with cerebral metastases from malignant melanoma. In the latter patient there was no increase in number or size of brain metastases while she received AR for 9+ months. In the teratoma patients 3 showed a rise in beta-hCG (beta human chorionic gonadotropin) and 3 a rise in AFP (alpha fetoprotein) during AR therapy. One teratoma patient had a laparotomy before and a thoracotomy after 9 weeks of AR. Histology showed similar undifferentiated tumor at both operations. Although hypervitaminosis A was well tolerated in these patients, it only stablized disease in 2/18 patients. (no Refs)

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STRUCTURE/ IDENTIFICATION/ CHARACTERIZATION

1. MONOCLONAL ANTIBODIES TO HUMAN PROSTATE AND BLADDER TUMOR-ASSOCIATED ANTIGENS.

Starling JJ, Sieg SM, Beckett ML, Schellhammer PF, Ladaga LE, Wright GL

Dept. Biochemistry, Eastern Virginia Medical Sch., Norfolk, VA, 23501

Cancer Res; 42(8):3084-3089 1982

Monoclonal antibodies to human prostate adenocarcinoma membrane antigens were produced by fusion of P3X63/Ag8 mouse myeloma cells with spleen cells from BALB/c mice immunized against the prostate cancer cell line DU145. The hybrids were screened for antibody production using glutaraldehyde-fixed cells in a solid-phase radioimmunoassay. Antibody-binding specificity was also checked by quantitative adsorption, membrane immunofluorescence, and complement-dependent cytotoxicity assays. A hybridoma clone (83.21) was isolated that secreted antibodies which preferentially bound to several prostate and bladder cancer cell lines but did not bind to a variety of other normal and malignant human cell lines. This antibody also reacted with a cytomegalovirus-transformed human embryonic lung cell line but not to normal human embryonic lung cells. Quantitative adsorption studies demonstrated that the 83.21 monoclonal antibody was strongly reactive to membrane preparations from human prostate adenocarcinoma tissue and a liver metastasis of prostate carcinoma. Little or no binding activity was observed against two other prostate carcinomas, benign prostatic hyperplasia, normal prostate, or normal liver. Binding studies indicate that the 83.21 monoclonal antibody does not bind to alpha-fetoprotein, carcinoembryonic antigen, prostatic acid phosphatase, human leukocyte antigen, Beta2-microglobulin, HLA-Dr antigens, fibronectin, or prostate antigen. The data indicate that we have isolated a monoclonal antibody that binds to an antigen(s) expressed by several urogenital carcinoma cell lines as well as human prostate tumor tissue and that the antibody is not directed against well-known human tumor cell markers. (Author abstract) (37 Refs)

ASSAY PROCEDURES/ SYNTHESIS

2. ESTABLISHMENT AND CHARACTERIZATION OF TWO NEOPLASTIC CELL LINES (U-1285 AND U-1568) DERIVED FROM SMALL CELL CARCINOMA OF THE LUNG.

Bergh J, Larsson E, Zech L, Nilsson K
Wallenberg Lab., Univ. Uppsala, Box 652, 751 22 Uppsala, Sweden
Acta Pathol Microbiol Scand [A]; 90(3):149-158 1982

Two human cell lines have been established in vitro from patients with small cell carcinoma of the lung (SCC). The U-1285 line was derived from the classical small cell type of SCC while the U-1568 originated from a larger cell variant. The cell lines grow as suspension cultures and have been passaged continuously in vitro for 3 yr (U-1285) and 2 yr (U-1568), respectively. The malignant nature of the lines is suggested by their infinite growth potential, their capacity to form colonies in agarose and their aneuploidy. Both cell lines contain cytoplasmic electron dense particles indistinguishable from classical neurosecretory granules but only in U-1568 has hormone production (human chorion gonadotropin (alpha-HCG)) been proven. The U-1568 line produces carcino-embryonic antigen (CEA) while both U-1285 and U-1568 produce alpha-feto-protein (AFP). Chromosome analysis reveal aneuploidy of both lines. Among structural aberrations, involvement of chromosome 14 in U-1285 and chromosomes 1, 7 and 12 in U-1568 is interesting since alterations of these chromosomes have been described previously in other malignant conditions. (Author abstract) (44 Refs)

3. DIFFERENTIAL RESPONSES TO X-IRRADIATION OF SUBPOPULATIONS OF TWO HETEROGENEOUS HUMAN CARCINOMAS IN VITRO.

Leith JT, Dexter DL, DeWyngaert JK, Zeman EM, Chu MY, Calabresi P, Glicksman AS
Box G, Brown Univ., Providence, RI, 02912
Cancer Res; 42(7):2556-2561 1982

The responses of two heterogeneous human cancer cell lines and their derivative clones to graded single doses of x-rays were examined in vitro. One system consisted of the human colon carcinoma line DLD-1 and two subpopulations (clones A and D). The second system consisted of the human lung carcinoma line (LX1) and four subpopulations (LX1-1, LX1-2, LX1-3 and LX1-9). These subpopulations have previously been shown to be markedly heterogeneous in terms of such characteristics as karyotype, morphology, drug sensitivity, tumorigenicity, and expression of membrane glycoproteins (such as carcinoembryonic antigen and tumor colonic mucoprotein antigen). Exponentially growing cultures were irradiated with graded single doses of 100-kVp x-rays. Survival was assessed using colony formation as the end point, and responses from multiple experiments were fitted to the single-hit, multitarget equation of cell survival. Values for the mean lethal dose (Do, grays), quasithreshold dose (Dq, grays), and extrapolation number (n) were obtained. For the human colon adenocarcinoma system, these values for the three tumor lines were: DLD-1, 0.95, 2.34, and 11.7; clone A, 1.06, 2.23, and 8.20; and clone D, 1.08, 1.89, and 5.80. For the human lung carcinoma system, these values for the five sublines were: LX1, 1.14, 0.19, and 1.20; LX1-1, 0.96, 2.06, and 8.54; LX1-2, 0.96, 0.88, and 2.48; LX1-3, 0.68, 2.05, and 20.3; and LX1-9, 1.12, 0.00, and 1.00. These two human tumor systems therefore exhibit variability in their intrinsic sensitivity to x-irradiation. The data indicate that failure of some human carcinomas to respond to physical treatment modalities can be due to preexisting resistant subpopulations. (Author abstract) (43 Refs)

4. STUDIES ON ESTABLISHMENT OF A HUMAN MALE GERM CELL AFP-PRODUCING TUMOR LINE (JTG-1) IN NUDE MICE FROM HUMAN TESTICULAR TUMOR (EMBRYONAL CARCINOMA WITH SEMINOMA) AND ITS CHARACTERISTICS.

Machida T, Miki M, Yanagisawa M
Dept. Urology, Jikei Univ. Sch. Medicine, Tokyo, Japan
Nippon Hinyokika Gakkai Zasshi; 72(12):1527-1533 1981

The establishment of a human male germ cell tumor line (JTG-1) in nude mice is reported. Tumor take was 100% and no spontaneous regression was observed. Levels of alpha-fetoprotein (AFP) increased in the serum and cystic fluids of the mice, indicating that this is an AFP-producing tumor. Characteristics of the original tumor (human testicular tumor) were thought to have changed at the first transplantation to those of a yolk sac tumor, but the characteristics of the tumor did not change during the 36 serial transplantations in nude mice accomplished to date. (13 Refs) (In JPN)

5. ESTABLISHMENT AND CHARACTERIZATION OF TWO HUMAN PANCREATIC CANCER CELL LINES TUMORIGENIC IN ATHYMIC MICE.

Dexter DL, Matook GM, Meitner PA, Bogaars HA, Jolly GA, Turner MD, Calabresi P
Dept. Medicine, Roger Williams General Hosp., 325 Chalkstone Ave., Providence, RI, 02908
Cancer Res; 42(7):2705-2714 1982

Two human pancreatic cancer lines, RWP-1 and RWP-2, have been established from two patients with primary pancreatic cancer metastatic to the liver. The patients' tumors, the xenografted tumors, and tumors obtained by inoculation of nude mice with cultured RWP-1 and RWP-2 cells are all moderately-well-differentiated ductal cell adenocarcinomas. Ultrastructural analysis supports the tissue histopathology findings. Xenografts of RWP-1 tumors double every 10 days, whereas the doubling time of RWP-2 xenografts is 22 days. Both tumors contain mucin. RWP-1 and RWP-2 cells have a doubling time in culture of 45 hr and form colonies in soft agar. RWP-1 cultures appear to be morphologically heterogenous; two distinct epithelial cell types can be identified. RWP-1 and RWP-2 have modal chromosome numbers of 64 and 62, respectively. Appreciable levels of glucose-6-phosphate dehydrogenase and lactic dehydrogenase were found in both cell lines and xenografts. RWP-1 and RWP-2 cells produce appreciable amounts of carcinoembryonic antigen, 1,090 and 414 ng/10(6) cells, respectively. (Author abstract) (51 Refs)

6. ESTABLISHMENT OF AN EXPERIMENTAL MODEL OF HUMAN HEPATOBLASTOMA.

Hata Y, Uchino J, Sato K, Sasaki F, Une Y, Naito H, Manabe K, Kawahara T, Kasai Y
Hokkaido Univ. Sch. Medicine, N-14, W-5, Sapporo, Japan
Cancer; 50(1):97-101 1982

Establishment of xenografts or cell culture lines in which the alpha-fetoprotein (AFP) characteristic of clinical hepatoblastoma persists have been difficult. The serially transplantable strain (HB-3) of highly AFP-producing hepatoblastoma was successfully established in nude mice. And a highly AFP producing cell line (c-HB-3) is easily obtained by HB-3. This strain and line give us an ideal experimental model of hepatoblastoma in vivo and in vitro. (Author abstract) (7 Refs)

7. EFFECT OF THE ANTI-HUMAN AFP-SPECIFIC ANTIBODY ON AFP-PRODUCING TUMOR LINE (JTG-1) IN NUDE MICE.

Yanagisawa M, Machida T, Hirai H
Dept. Urology, Jikei Univ. Sch. Medicine, Tokyo, Japan
Nippon Hinyokika Gakkai Zasshi; 72(12):1569-1576 1981

JTG-1 tumor-bearing nude mice were administered anti-human alpha-fetoprotein specific antibody (AAFPSA; 1.8 mg, 2x/wk x 4), and the effects of the AAFPSA on the tumors were observed. Alpha-fetoprotein levels in the serum and cystic fluid of the mice administered the AAFPSA were lower than those in the control groups, and more tumor necrosis was observed in the mice given AAFPSA. (25 Refs) (In JPN)

8. A NEW HUMAN COLON TUMOR CELL LINE, LS123 (MEETING ABSTRACT).

Rutzky LP, Siciliano MS, Giovanella BC, Noguchi PD, Kahan BD
The University of Texas Medical School and System Cancer Center, Houston, TX
In Vitro; 18(3,part2):294 1982

An epithelial cell line, LS123, was established in 1974 from the second of a series of three primary colon tumors resected from a Caucasian female. The tumor was a Dukes' B adenocarcinoma. Allozyme phenotyes of polymorphic enzyme loci had a frequency of 4x10(-3) and confirmed the independent genetic origin of this line. Although the line is heteroploid, it failed to display some properties associated with malignancy. Progressive tumors did not develop following inoculation of either 1 or 2x10(7) cells into N:NIH(S)II or nu/nu Swiss nude mice, respectively. Colonies developed in the Hamburger-Salmon stem cell assay system, but not in 0.3% Bacto, Noble or agarose agars. LS123 cells formed colonies on confluent cell monolayers and were capable of serial growth in serum-free medium. Low concentrations of the tumor marker carcino-embryonic antigen (CEA) of 14.5x10(-5) ng CEA/cell were detected after 21 days of incubation. LS123 cells were invasive in the Chick Embryonic Skin assay system. Nests of glandular structures were observed in the skin, but little mitotic activity was present. The cells were well differentiated and resembled an abnormal colonic epithelium. (no Refs)

9. ESTABLISHMENT OF A HUMAN TUMOR CELL LINE FROM A PATIENT WITH PRIMARY HEPATOCELLULAR CARCINOMA (MEETING ABSTRACT).

He L, Wands JR, Quarcoi A, Isselbacher KJ
Gastrointestinal Unit, Massachusetts General Hospital, Boston, MA, 02114
Gastroenterology; 82(5,part2):1080 1982

A tumor cell line designated CUSPF (China-United States Peoples Friendship) was established in long-term culture from a hepatitis B surface antigen (HBsAg) negative individual with a poorly differentiated primary hepatocellular carcinoma. The cultured cells have an epithelioid appearance by light and phase contrast microscopy. Scanning electron microscopy revealed extensive microvilli formation on the cell surface as well as communications between cells. Transmission electron microscopy demonstrated a polygonal morphology, with 'epithelioid like' junctions between cells, numerous mitochondria and smooth endoplasmic reticulum, but a poorly developed rough endoplasmic reticulum. Growth curves repeated three months apart were identical and demonstrate a doubling time of 48 hours. The CUSPF cells show loss of contact inhibition under confluent conditions. Human chromosomes were identified by isoenzyme analysis. The cells were shown to have aspartate aminotransferase (SGOT) activity but do not synthesize or secrete HBsAg or alpha fetoprotein. Monoclonal antibodies have been prepared to this cell line. The malignant potential of the CUSPF cell line was established by gross tumor formation when injected subcutaneously (1.4x10(7)) into nude mice. The morphology of the solid tumor closely resembles the original hepatocellular carcinoma. Finally, the properties of recultured cells derived from the solid tumor mass grown in nude mice appear to be identical to the original CUSPF cell line. Thus, we have established in culture a human hepatocellular carcinoma cell line. Such cells will be of use in characterization of the malignant properties of human hepatocytes. (no Refs)

10. SUBCELLULAR DISTRIBUTION, SYNTHESIS, AND RELEASE OF CARCINOEMBRYONIC ANTIGEN (CEA) IN CULTURED HUMAN COLON CANCER CELL LINES (MEETING ABSTRACT).

Shi ZR, Tsao D, Kim YS
GI Research Laboratory, Veterans Administration Medical Center, San Francisco, CA, 94121
Gastroenterology; 82(5,part2):1178 1982

The wide range of serum CEA levels in patients with colon cancer has been attributed to various factors, including the content and turnover rate of cellular CEA. In this study the subcellular distribution, content and rate of synthesis and release of CEA were investigated in nine human colon cancer cell lines. Membrane and cytosol fractions were obtained by centrifugation at 100,000 x g for one hour and the CEA contents were determined by Hansen's radioimmunoassay method. More than 80% of CEA was membrane associated. The CEA content varied greatly among the cell lines studied. The well differentiated cell lines, LS174T and SKCO-1, displayed high CEA contents, 599.4 ng and 355.0 ng/10(6) cells respectively. The rate of CEA synthesis and release was studied by determining the CEA contents in the cultured cells and media at 24 hour intervals up to ten days. The rate of synthesis in LS174T, SKCO-1 at the stationary phase decreased to 20% and 50%, respectively, of that at the log phase. HCT48 had a rate of CEA synthesis 55-fold greater at stationary phase (109.1 ng/10(6) cells/day) than that at log phase (2.1 ng/10(6) cells/day). LS174T, SKCO-1 and HCT 48 all showed a higher rate of release of CEA at the stationary phase. The rate of synthesis of CEA was further studied by incubating the cells at the log and stationary phase with (N-acetyl-H3) glucosamine for five and 24 hours. The labeled CEA was immunoprecipitated with anti-CEA antisera from detergent solubilized cells and counted for radioactivity. LS174T showed a higher rate of synthesis of CEA at the log phase than that at stationary phase, and the opposite was found for HCT48. (no Refs)

11. EFFECT OF SODIUM BUTYRATE ON CARCINOEMBRYONIC ANTIGEN (CEA) PRODUCTION BY HUMAN COLONIC ADENOCARCINOMAS IN CULTURE (MEETING ABSTRACT).

Tsao D, Shi ZR, Kim YS
GI Research Laboratory, Veterans Administration Medical Center, San Francisco, CA, 94121
Gastroenterology; 82(5,part2):1199 1982

The expression of CEA in human colonic tumor has been related to the degree of differentiation. Human colonic tumor cell lines were treated with sodium butyrate, a differentiation inducing agent which is known to reduce in vitro tumorigenicity. There was a 10-20 fold increase of CEA activity in lines HRT-18 and HCT-48, and a 2-4 fold increase in lines LS174T and SKCO-1. Activity did not increase in lines SW480, SW620 and SW1116. The enhanced expression of CEA could be inhibited by the protein synthesis inhibitors cycloheximide and actinomycin-D. Neither the subcellular distribution of CEA nor the rate of release of CEA into culture medium by cells was changed by the treatment. Cell surface CEA was labeled with galactose oxidase, followed by reaction with sodium borotritide and subsequently immunoprecipitated specifically with anti-CEA antiserum. Examination of labeled membrane surface CEA from control and butyrate treated HCT48 and LS174T cells by SDS-(sodium dodecyl sulfate)-Polyacrylamide gel electrophoresis (PAGE) revealed a major glycoprotein of 200,00 dalton molecular weight, indicating that no new form of CEA was induced with sodium butyrate treatment. The membrane-associated CEA was identified with rabbit anti-CEA antiserum and 125I-Protein A on nitrocellulose paper after the cell membrane proteins had first been separated by SDS-PAGE and transferred to the paper; again, the control and butyrate-induced CEA were similar. Lectin affinity chromatography of cellular CEA revealed a higher binding of CEA from butyrate-treated HCT48 cells to RCA-Sepharose 4B than that from untreated cells. (no Refs)

12. TOXICITY OF MULLERIAN INHIBITING SUBSTANCE TO CELLS DERIVED FROM A HUMAN ENDOMETRIAL TUMOR (MEETING ABSTRACT).

Price JM
Department of Obstetrics and Gynecology, University of Massachusetts Medical Center, Worcester, MA, 01605
In Vitro; 18(3,part2):323 1982

A cell line (HEC-1A) derived from a human endometrial tumor is responsive to the presence of Mullerian Inhibiting Substance (MIS) when grown in McCoy's medium in the absence of serum but with the addition of insulin (5 ug/ml), transferrin (5 ug/ml), hydrocortisone (50 nM), EGF (epidermal growth factor) (10 ng/ml) and FGF (fibroblast growth factor) (50 ng/ml). These cells exhibit a 40% reduction in the incorporation of 3H-TDN within 12 h following the addition of MIS to the cultures when compared to similar cultures without MIS. Cells maintained in McCoy's medium with 15% fetal bovine serum show no response to MIS. Other experiments indicate that serum does not inhibit the action of MIS. MIS, isolated for these experiments from neonatal calf Sertoli cells, is a testicular glycoprotein which causes the involution of the Mullerian duct during development of the male fetus. Because the Mullerian duct is the anlage of the uterus and uterine tubes in mammals, it is postulated that cells derived from tumors of Mullerian duct origin must reacquire a sensitivity to the action of MIS by presence of fetal antigens on their cell surface. Additionally, serum must inhibit either the formation or expression of these antigens. (no Refs)

EXPERIMENTS IN ANIMAL SYSTEMS

13. ISOLATION OF RAT ALPHA-FETOPROTEIN FROM MORRIS HEPATOMA 7777.

Bereta J, Koj A
Lab. Enzymology, Inst. Molecular Biology, Jagiellonian Univ., Grodzka 53, 31-001 Krakow, Poland
Int J Biochem; 14(7):641-648 1982

A reliable method was developed for the isolation of alpha-fetoprotein (AFP) from Morris hepatoma 7777 after tumor incubation in vitro. The procedure included salting out with ammonium sulfate, affinity chromatography (CR) with either concanavalin A-Sepharose or Cibacron-Blue-Sepharose, hydrophobic CR and preparative polyacrylamide gel electrophoresis (PAGE). Approx yield of pure AFP was 10% as judged from crossed immunoelectrophoresis and sodium dodecyl sulfate-PAGE. (17 Refs)

14. EFFECT OF THE TIME OF CYCLOPHOSPHAMIDE ADMINISTRATION ON THE RHYTHM OF ALPHA-FETOPROTEIN LEVEL IN THE SERUM OF MICE WITH HEPATOMA 22A AND PROLIFERATION OF TUMOR CELLS.

Romanov IuA, Piaksina TI, Filippovich SS
Dept. Biology, Medico-Biological Faculty, N. I. Pirogov Second Medical Inst., Moscow, USSR
Biull Eksp Biol Med; 93(4):73-75 1982

Diurnal rhythms of serum level of alpha-fetoprotein (AFP) and of proliferative activity of tumor cells were studied in male C3HA mice with transplanted hepatoma 22A. On day 4 after tumor transplantation, animals were subjected to a single sc inoculation with cyclophosphamide (CP: 150 mg/kg). CP was administered at 11 am, 5 pm, 11 pm, and 5 am. CP administration delayed the appearance and reduced the level of AFP. The most pronounced changes in AFP levels were observed after CP administration at 11 pm and at 5 am. CP produced mild inhibition of the proliferative activity of hepatoma 22A cells. (7 Refs) (In RUS)

15. ALPHA-FETOPROTEIN SYNTHESIS DURING EARLY STAGES OF HEPATOCARCINOGENESIS IN MICE WITH DIFFERENT SENSITIVITY TO ORTHO-AMINOAZOTOLUENE.

Serova IA, Kaledin VI, Kostyrev OA, Gruntenko EV
Inst. Cytology and Genetics, Novosibirsk, USSR
Dokl Akad Nauk SSSR; 263(5):1245-1249 1982

Alpha-fetoprotein (AFP) synthesis during ortho-aminoazotoluene (OAT) induced liver carcinogenesis was studied in OAT-sensitive DD/He, DBA/2J, CBA/LacSto, and A/He mice and in OAT-resistant CC57BR/Mv and BALB/cLacSto mice. The ip or sc administration of OAT produced marked necrotic changes in the liver of sensitive mice. Resistant mice and sensitive CBA mice did not show morphological changes in the liver tissue. Both sensitive and resistant mice showed the first peak of AFP on day 4 after OAT administration. The resistant mice showed normalization of AFP blood levels, while the sensitive mice developed the second increase of AFP level. (10 Refs) (In RUS)

16. GROWTH OF MURINE SARCOMA AND MURINE XENOTROPIC LEUKEMIA VIRUSES IN JAPANESE QUAIL: INDUCTION OF TUMORS AND DEVELOPMENT OF CONTINUOUS TUMOR CELL LINES.

Robey WG, Kuenzel WJ, Vande Woude GF, Fischinger PJ
Lab. Viral Carcinogenesis, NCI, Frederick, MD, 21701
Cancer Res; 42(7):2523-2531 1982

The BALB/c murine endogenous xenotropic leukemia virus pseudotype of m1 Moloney sarcoma virus [m1MSV(B-MuX)] was used to productively transform diploid Japanese quail embryo cells. The majority of newly hatched quail inoculated with m1MSV(B-MuX)-transformed quail embryo fibroblast cells rapidly developed tumors which were predominantly locally invasive fibrosarcomas, but metastases were observed in two birds. In two tumor-bearing quail, lymphosarcomas were observed in conjunction with fibrosarcomas. Quail inoculated with m1MSV(B-MuX) virus or quail embryo fibroblast cells infected with helper leukemia virus did not develop tumors. A cell culture derived from one quail tumor was shown to be oncogenic in newly hatched quail. Viruses produced by m1MSV(B-MuX)-infected quail cells or quail tumors had envelope properties of BALB-derived murine xenotropic leukemia virus as measured by host range, interference, and neutralization. Virus structural antigens, proteins with mol wt of 30,000 and 70,000, were detected in tumors and tumor-derived cell lines by immunofluorescence and gel diffusion. Sera from tumored quail had high titers of type-specific BALB-derived murine xenotropic leukemia virus antibodies as determined by neutralization and immunoprecipitation. Antibodies to the putative m1 Moloney sarcoma virus V-mos gene product were not detected in sera from tumored or regressor quail. (Author abstract) (41 Refs)

IMMUNOLOGIC INTERACTIONS

17. THE LEUKOCYTE ADHERENCE INHIBITION TEST IN TUMOR PATIENTS USING 3 M KCL EXTRACTS OF FETAL TISSUES AS ANTIGENS.

Albrecht S, Schlott B, Pasternak G, Reinhofer J, Lunow G
Zentralinstitut fur Krebsforschung, Lindenberger Weg 80, DDR-1115 Berlin-Buch, E. Germany
Arch Geschwulstforsch; 52(5):341-348 1982

The sensitivity of tumor patients to 3 M KCl extracts of fetal tissues was tested using the lymphocyte adherence inhibition (LAI) test. Blood samples were obtained from patients with mammary, gastric, lung, colorectal, gynecological, or other types of carcinomas. Blood from blood donors, clinical and laboratory personnel, patients with benign diseases, and healthy persons served as controls. The 3 M KCl extracts were prepared from whole fetuses obtained by abortion at 1-3 mo gestation and from fetal organs (liver, lung, spleen, kidney, and heart) obtained by abortion at 5 or 7 mo gestation. LAI tests were performed using 10(6) lymphocytes and 100-300 ug of extract incubated at 37 C for 2 hr. Positive reactions by lymphocytes from tumor patients were obtained in 12/18 tests with 1-3-mo extracts, 13/15 with 5-mo extracts, and 14/16 with 7-mo extracts, compared to 5/20, 4/15, and 1/19, respectively, in controls. Sensitivity to 7-mo extracts was found in 8/13 pregnant women. Sensitivity to human encephalitogenic protein was shown by 3/14 controls, 10/11 tumor patients, and 3/5 pregnant women. Sensitivity to fetal antigens was shown by patients bearing each type of tumor; no organ restriction was found. Although results of the LAI are not suitable for diagnosing individual patients, LAI is useful for studying antigen preparations. (45 Refs)

18. EFFECTS OF HETEROLOGOUS ANTISERA TO RAT ALPHA-FETOPROTEIN ON GROWTH OF CULTURED FETAL RAT HEPATOCYTES.

Watabe H, Tsuji Y, Saito T
Dept. Biochemistry, Faculty of Pharmaceutical Sciences, Higashi-Nippon-Gakuen Univ., Ishikari-Tobetsu, Hokkaido 061-02, Japan
Tumor Res (Sapporo); 16:29-36 1981

The effect of heterologous antisera to alphafetoprotein (AFP) on the growth of cultured fetal rat hepatocytes which produce AFP and other serum proteins was investigated. Horse anti-AFP induced marked inhibition of cell growth compared to both normal horse and fetal calf sera. Inhibition by anti-AFP horse serum 5 days after plating was 83.3%. Rabbit anti-AFP serum was inhibitory to cell growth as well, although to a much lesser degree than horse anti-AFP. Goat anti-AFP serum treatment had little effect on cultures even when the concentration of antiserum was raised to 20%. Both antisera from rabbit and goat showed non-specific recovery efficiency on hepatocyte growth. An inhibitory effect was observed even when horse anti-AFP was added 2 days after plating. Enhancement of cell growth was observed in cultures treated with normal horse serum. Rabbit anti-albumin serum was not growth inhibitory even at high concentrations. Cells treated with horse anti-AFP showed faint immunoperoxidase staining of AFP and albumin, irregularity of the cell periphery, and many dead cells adhering to the dyes. These results are consistent with cell killing induced by the antisera. (27 Refs)

19. THE OCCURRENCE OF CANCER IN IMMUNE DEFICIENCIES.

Penn I
Dept. Surgery, Univ. Colorado Health Sciences Center, Denver, CO
Curr Probl Cancer 6(10): 64 pp., 1982.

The association of immune deficiency states with increased cancer risk is discussed in detail. Topics covered include components of the immune system (specific immune responses, B cells, T lymphocytes, delayed hypersensitivity cells, cytotoxic T cells, helper T cells, and suppressor T cells), immune amplification mechanisms, nonspecific responses (humoral response, cellular response), immune responses to cancer (reactions deleterious to tumor growth, reactions favoring tumor growth [blocking factors, fetal antigens, alpha2-globulins, small mol wt immunosuppressive factors, suppressor cells, lack of complement]). Also discussed are mechanisms by which tumors escape immune destruction by the host, cancer in immunodeficient states, naturally occurring immunodeficient states, changes associated with organ transplantation (immunosuppressive therapy, transplanted malignancies, cancers arising de novo after organ transplantation [incidence, age and sex of patients, time of appearance of cancers, previous tumors in recipients, malignancies in the donors, types of malignancy]), multiple cancers, treatment, prognosis, effects of immunosuppression on preexisting neoplasms, cancer in uremic patients, second neoplasms arising in patients after cancer chemotherapy and radiotherapy, etiology of neoplasms in immunodeficient states, spontaneous regression of lymphomas, interferons, oncogenic viruses, oncogenic and co-oncogenic effects of immunosuppressive and cancer chemotherapeutic agents, and other potentially oncogenic treatments. (265 Refs)

CLINICAL/ DIAGNOSIS/ IMMUNOTHERAPY

20. ANALYSIS OF CASES OF HEPATIC CELL CARCINOMA THAT TRANSFORMED FROM VIRAL HEPATITIS.

Ichida F, Honma A, Soga K
Third Dept. Internal Medicine, Niigata Univ. Sch. Medicine, Niigata, Japan
Nippon Rinsho; 40(2):468-477 1982

World epidemiological surveys and molecular biology research on the relationship between hepatitis B virus (HBV) and liver cancer are discussed, and cases of hepatitis and hepatic cirrhosis which transformed into hepatic cancer in Japanese patients are analyzed. Various epidemiological and molecular biology studies show a clear correlation between HBV and hepatic cell carcinoma. Patients with B-type hepatitis, cirrhosis, or hepatic cancer were significantly younger than those with non-B type hepatitis, cirrhosis, or hepatic cancer, respectively. Approx 70% of 110 cases of hepatic cancer were found to have positive laboratory findings related to HBV. The patients who had chronic liver disease and who were positive for hepatitis Bs (HBs) antigen were thought to be at high risk for developing hepatic cancer. No direct relationship was observed between alpha-fetoprotein (AFP) levels and serum HBs antigens, however, monitoring levels of AFP was thought to be an important method to help detect early stage liver cancer. (33 Refs) (In JPN)

21. EARLY STAGE CANCER DIAGNOSIS SYSTEM FOR MINUTE HEPATOCELLULAR, CHOLEDOCHAL, AND PANCREATIC CANCERS: CURRENT CAPABILITIES AND PROBLEMS.

Okuda K, Tsuchiya Y, Saisho H
First Dept. Internal Medicine, Chiba Univ. Sch. Medicine, Chiba, Japan
Nippon Rinsho; 40(1):146-150 1982

Patients at high risk for hepatic, choledochal, or pancreatic cancer and methods used in early detection of minute cancers are discussed. Patients at high risk of hepatic cancer include those with hepatic cirrhosis and who are positive for hepatitis B-virus surface antigen (HBsAg), those with a history of HBsAg negative cirrhosis and had transfusions or surgery, those with a long history of chronic hepatitis, and those with Budd-Chiari disease. Methods used to diagnose early stage hepatocellular cancer include testing for alpha-fetoprotein, ultrasonography, computed tomography, 99mTc scintigraphy, and abdominal angiography. Choledochal cancer has been primarily detected with choledochal roentgenography, but real time ultrasonography is being used more often. Ultrasonography is useful in detecting eruptive-type gall bladder cancers but not the flat-type. Gall bladder tumors greater than 10 mm can be diagnosed as malignant, and the 8-10 mm tumors are potentially malignant. When roentgenograms are negative for gall bladder disease, ultrasound-guided puncture biopsy might be performed. Distinctive features of pancreatic cancers observed with the aid of ultrasonography include an enlarged localized tumor, a low-echo localized within the parenchyma or an inconsistent echo level in a spherical shape, and numerous spherical dilations of the pancreatic duct. (8 Refs) (In JPN)

22. EPIDEMIOLOGY, EARLY DIAGNOSIS AND TREATMENT OF LIVER CELL CANCER.

Tsung-Tang S, Zhao-You T, Yuan-Yun C
Cancer Inst., Chinese Acad. Medical Sciences, Beijing, People's Republic of China
Gastrointestinal Cancer 1. Decosse JJand Sherlock P, ed. The Hague, Martinus Nijhoff Publishers, Cancer Treatment and Research, Vol. 3, 452 pp., 1981.

Possible etiological factors, mechanism of carcinogenesis, early diagnosis, and surgical treatment of liver cell cancer are reviewed. Topics include epidemiology (geographic distributions, hepatotoxins, hepatitis B virus, host factors, prevention trials), early diagnosis (alpha fetoprotein serology, hepatoangiography, ultrasonography, computerized tomography, radionuclide imaging, tumor markers other than alpha fetoprotein), and treatment (early treatment of mass survey patients and ultimate outcome, surgical resection, surgical approach to nonresectable cases, conservative treatment of liver cell cancer). (147 Refs)

23. DIAGNOSTIC VALUE OF ALPHA-FETOPROTEINS (AFP).

Weck M
Medizinische Klinik, Medizinische Akademie 'Carl Gustav Carus' Dresden, Fetscherstrasse 74, DDR-8019 Dresden, E. Germany
Z Aerztl Fortbild (Jena); 76(4):165-168 1982

The diagnostic value of measurements of alpha-fetoprotein (AFP) is reviewed. AFP measurements are indicated for suspected hepatocellular carcinoma or teratogenic tumor, postoperative monitoring of AFP-positive tumors, control of radio- or chemotherapy of AFP-positive tumors, detection of malignant transformation of cirrhosis of the liver, monitoring of the course of pregnancy, and prenatal diagnosis of certain fetal malformations. AFP measurements must be interpreted in conjunction with other findings. (In GER)

24. PROGNOSTIC VALUE OF PREOPERATIVE SERUM CEA LEVEL COMPARED TO CLINICAL STAGING: II. STOMACH CANCER.

Staab HJ, Anderer FA, Brummendorf T, Hornung A, Fischer R
Friedrich Miescher Laboratorium, Max Planck Gesellschaft, Spemannstr. 37-39, 7400 Tubingen, W. Germany
Br J Cancer; 45(5):718-727 1982

In a clinical investigation of postoperative survival after primary surgery for stomach cancer, 390 patients were registered since 1974. The potential prognostic parameters examined within the first days of hospitalization for primary resection included age of the patients, operability, tumor extension (TNM classification) and tumor Stages I-IV (UICC). Statistical treatment of the data revealed that each of the clinical parameters covers critical ranges associated with highly significant differences in patient survival. The preoperative serum CEA concentration exhibited prognostic significance in addition to the criteria of operability and tumor extension. In selected subgroups of patients with distinct resectability and tumor extension, ranges of preoperative CEA concentration could be specified which were associated with statistically significant differences in the patient survival. The results indicate that the preoperative serum CEA level can be an independent prognostic parameter in stomach cancer. (Author abstract) (15 Refs)

25. MODERN DIAGNOSIS OF PANCREATIC CARCINOMA.

Soehendra N, Klapdor R, Lehmann U, Schmiegel WH, Brockmann wP, Vogel H, Kloppel G

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Med Klin; 77(9):289-293 1982

Modern possibilities for the diagnosis of pancreatic carcinoma are described and personal experience with diagnosis in 32 patients is reported. In the 32 patients with confirmed primary pancreatic carcinomas, tumor was suggested by sonography in 19/21 cases, by computer tomography in 20, by endoscopic retrograde cholangiopancreaticography (ERCP) in 28, by cytological examination in 4, by the determination of oncofetal antigen in 4, and by analysis of pancreatic juice in 0.20 samples examined. ERCP was found to be the most reliable diagnostic method, while sonography is recommended as a preliminary diagnostic examination. Sonography and computer tomography are suitable for detecting pancreatic tumors with min diameters of 1.5-2 cm. Computer tomography was found to be best for the diagnosis of hepatic metastases, but it was not possible to detect all hepatic metastases even by the combination of computer tomography, sonography and angiography, ie, laparoscopy or staging laparotomy was sometimes necessary. Pancreatic carcinoma is still diagnosed mostly too late, and the resection rate is below 20%. (17 Refs) (In GER)

26. CARCINOEMBRYONIC ANTIGEN (CEA) IN BREAST CANCER.

Catania G, Azzarello G, Di Stefano A, Cardi F, Basile F, Iuppa A, Mazzarino C

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Minerva Chir; 37(5):465-470 1982

The CEA levels were determined in 40 women with breast cancer before and after 3 yr after treatment consisting of surgery, postoperative chemotherapy with cyclophosphamide and telecobalt therapy (total dose 4,000-4,600 rads/field in 30 sessions). The patients in Stage III were also treated with medroxyprogesterone acetate (MAP), and all patients with estrogen receptors were treated with Tamoxifen. Stage I was diagnosed in 15/40 patients, II in 17 and III in 8. The patients in Stage I had CEA levels measured before treatment, and they were above 20 nanog (ng)/ml in 5/15 cases, between 10 and 20 ng/ml in 3/15 and below 10 ng/ml in 7/15. The CEA levels in the Stage II patients were above 20 ng/ml in 12/17 cases, 10-20 ng/ml in 4/17 and below 10 ng/ml in 1/17. The patients in Stage III had the CEA levels above 20 ng/ml in 6/8 cases. During the first mo after surgery the CEA levels dropped to normal levels in the Stage I and II patients and to 28-60 ng/ml in the Stage III patients. The reduced levels persisted in 9/15 patients in Stage I and in 12/17 in Stage II. The development of metastases in 2/3 patients in Stage I and in 1/3 in Stage II was preceded by a rise in the CEA levels several mo before manifestation. Constantly high CEA levels were measured in Stage III patients for 4 mo after surgery, but ovariectomy and Tamoxifen treatment caused a decrease to 15 ng/ml lasting for 3 yr at the time of reporting. (20 Refs) (In ITA)

27. CARCINOEMBRYONIC ANTIGEN AS A MONITOR OF RECURRENT BREAST CANCER.

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J Surg Oncol; 20(2):109-114 1982

Carcinoembryonic antigen (CEA) test was performed at the time of diagnosis in 136 patients with early operable breast carcinoma (Stage I = 65, Stage II = 71). Only 4% had CEA levels greater than 5 ng/ml. Patients with axillary metastasis (Stage II) had higher incidence of abnormal CEAs than those with disease localized to the breast (Stage I). Follow-up CEA tests were performed on 243 patients after mastectomy. In this group, 50 patients developed recurrent disease and 48% had elevated CEA levels. Patients with chest-wall recurrences rarely had abnormal CEAs, while those with visceral metastasis had higher levels. Among the 193 patients known to be without recurrence, 10% also had elevated CEAs. Excluding inflammatory, hepatic, and renal diseases, the most common medical conditions which could explain such false elevations are diabetes, hypertension, and organic heart disease. (Author abstract) (22 Refs)

28. ADEQUACY OF ESTROGEN SUPPRESSION WITH AMINOGLUTETHIMIDE AND HYDROCORTISONE AS TREATMENT OF HUMAN BREAST CANCER: CORRELATION OF HORMONAL DATA WITH CLINICAL RESPONSES.

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Cancer Res; 42(8,Suppl):3397s-3401s 1982

Human breast neoplasms can be divided into hormone-dependent and hormone-independent subtypes. Estrogen is the major hormonal stimulus for growth of the dependent tumors. Failure to respond to estrogen suppression therapy could reflect either an incomplete lowering of estrogens or the hormonal independence of the tumor. We compared the levels of several estrogens and other hormones in women experiencing objective responses and disease progression during therapy with the aromatase-steroidogenesis inhibitor, aminoglutethimide, and replacement hydrocortisone. Pretreatment hormonal profiles of the estrogens, androgens, ketosteroids, thyroxine, polypeptide hormones, and carcinoembryonic antigen did not differ significantly among response groups. During treatment, the levels of all estrogens were suppressed to a similar degree in the progression group and in the responders. Data suggested that lack of estrogen suppression did not explain the response to treatment in the patients receiving aminoglutethimide-hydrocortisone. This finding differs from our results in a similarly analyzed control group of patients treated with surgical adrenalectomy. Levels of the weak androgens, dehydroepiandrosterone sulfate and androstenedione, were found to be higher in the progression group compared to the responders. This observation could not be explained by differences in duration of treatment between groups. Analysis at 1 to 12 wk, 13 to 24 wk, and 25 to 36 wk after initiating treatment indicated higher androgen levels at each time point in the progression group. While the finding of higher androgen levels in the responder group remains unexplained, this study indicates that incomplete estrogen suppression is not responsible for lack of tumor response in patients with progressive disease during aminoglutethimide-hydrocortisone therapy. (21 Refs)

29. ANAPLASTIC SMALL-CELL BRONCHIAL CANCER.

Amiel JL, Ruffie P
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Nouv Presse Med; 11(20):1539-1541 1982

Histology, frequency, clinical symptoms, progression, and treatment of anaplastic small-cell bronchial cancer (ASBC) are discussed. Differential diagnosis of ASBC is considered. ASBC is often the cause of paraneoplastic syndromes such as Schwartz Bartter syndrome, lacks biological markers such as carcinoembryonic antigen, and seems to be underdiagnosed. It has been suggested that 20% of bronchial cancers are ASBC. ASBC is the bronchial cancer most clearly the result of cigarette smoking. The incidence of ASBC is increasing. ASBC is already responsible for more deaths than all hematosarcomas combined. The 5-yr survival rate for ASBC patients is 1%. Clinical manifestations of ASBC include vena cava compression, cervical adenopathies, and pleural effusion. Extrathoracic metastases are present in 84% of ASBC patients. The existence of metastases is of prognostic importance but does not alter the therapeutic approach. Combination chemotherapy for ASBC is described. When some of the chemotherapy regimens have been used, the median survival of certain ASBC patients has been increased from 3 mo to about 10 mo. (11 Refs) (In FRE)

30. SERUM BETA2-MICROGLOBULIN AND OTHER 'TUMOR ASSOCIATED' ANTIGENS IN PATIENTS WITH BRONCHOGENIC CARCINOMA.

Mordasini C, Riesen W, Morell A
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Lung; 160(4):187-194 1982

Quantitative determination of beta2-microglobulin (b2m), carcinoembryonic antigen (CEA) and alphafetoprotein (AFP) was made in 51 patients (mean 60 yr old) with bronchogenic carcinoma. Mean concentration of b2m in patients with bronchogenic carcinoma was 2.47 mg/liter (l), compared to 2.10 mg/l in patients with lung tuberculosis or other non-neoplastic lung diseases. Normal blood donors of similar age had a mean b2m concentration of 1.92 mg/l. Of patients with bronchogenic carcinoma, males had slightly higher b2m levels than females; concentrations greater than 2.4 mg/l b2m were observed in 24 patients. Lung cancer patients and normal blood donors showed distinct age dependent increases in b2m, the latter to a lesser degree. No clear correlation between histologic type of tumor and b2m level was observed. The longest survival time was noted in patients who did not have elevated levels of b2m. Of all individuals with a plasma b2m concentration greater than 3.0 mg/l, 9/10 had bronchogenic carcinoma. In 50 patients with histologically or cytologically proven bronchogenic carcinoma, b2m greater than 3.0 mg/l was observed in 9, CEA greater than 10 nanog/ml in 15, and AFP greater than 5 nanog/ml in 1. No patient had elevated b2m and CEA, and only one had elevated AFP and CEA. Combined determination of b2m and CEA gave 48% positive results, compared to 30% when CEA alone was determined. AFP determination did not increase the percentage of positive cases. (35 Refs)

31. URINARY CEA FOR PREDICTION OF SURVIVAL TIME AND RECURRENCE IN BLADDER CANCER.

Wahren B, Nilsson B, Zimmerman R
Dept. Virology, Natl. Bacteriological Lab., S-105 21 Stockholm, Sweden
Cancer; 50(1):139-145 1982

The prognostic information from carcinoembryonic antigen was evaluated in bacteria-free urines of patients with bladder carcinoma. Patients with elevated (greater than or equal to 30 ng/ml) U-CEA had a poorer relative and symptom-free survival than patients with initial U-CEA below 30 ng/ml. Patients in whom U-CEA decreased from before to after radiation treatment had a better survival rate than patients with increasing U-CEA. These findings were most significant in cases with large (T3 + T4) tumors or with tumors of a lower differentiation (G3). U-CEA appeared to be an independent variable for prognostic evaluation of survival, since these differences were also true within the subgroups of known variables such as classes or grades. All but one of the patients, in whom short-term local control was obtained, had a posttreatment U-CEA below 50 ng/ml. In oncology units, where the more malignant bladder tumors are treated, U-CEA determinations may indicate which patients require intensified monitoring or treatment. (Author abstract) (27 Refs)

32. TUMOR-ASSOCIATED ANTIGENS IN THE URINE OF PATIENTS WITH BLADDER CANCER.

De Fazio SR, Gozzo JJ, Monaco AP
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Cancer Res; 42(7):2913-2917 1982

Previous work in our laboratory has demonstrated that antisera to proteins found in the urine of bladder cancer patients can distinguish between urine samples from these patients and those from normal individuals when tested by a complement-fixation assay. Antisera which were reactive with individual tumor-associated antigens were used to detect the antigens in the urine of bladder cancer patients and control individuals. One antigen was found in 66% of the bladder cancer patients (n = 38) and 25% of control individuals (n = 20). This antigen is a glycoprotein with a molecular weight of about 200,000 and beta-electrophoretic mobility and is distinct from carcinoembryonic antigen. A second molecule detected by an antiserum to urine fractions proved to be completely identical to serum C-reactive protein. C-Reactive protein was found in the urine of 72% of the bladder cancer patients (n = 39) and 32% of the control population (n = 32). Although a third protein detected with these antisera proved to be a normal urinary component, two of these tumor-related proteins appear to have potential as diagnostic markers for bladder cancer. (Author abstract) (25 Refs)

33. ALPHA-FETOPROTEIN (AFP) AND HUMAN CHORIONIC GONADOTROPIN (HCG) AS TUMOR MARKERS IN CASES OF INTRACRANIAL AND INTRASPINAL GERM-CELL TUMORS.

Gjerris F, Peitersen B, Nielsen K, Arends J, Haase J, Lindholm J, Wewer U, Albrechtsen R
Neurokirurgisk afdeling 2092, Rigshospitalet, DK-2100 Copenhagen 0, Denmark
Ugeskr Laeger; 144(18):1296-1299 1982

Alpha-fetoprotein (AFP) and human chorionic gonadotropic (HCG) levels were determined in eight patients (4-28 yr old) with germ-cell tumors within the CNS. The tumors were localized in the pineal region in five patients, and in infratentorially, suprasellarly and lumbarly in one each. The tumors were classified histologically as germinomas, teratomas, yolk sac tumors, embryonic carcinomas and choriocarcinoma. All patients were subjected to surgery which was radical in 4/8, and to radiotherapy and two to additional chemotherapy. The serum AFP levels were elevated in 5/8 patients preoperatively and in 0/8 patients postoperatively. The AFP levels in the cerebrospinal fluid (CSF) were elevated in 1/3 patients tested preoperatively and in 0/3 postoperatively. The serum HCG levels were elevated in 4/8 patients preoperatively and in 5/5 patients postoperatively, even though elevated levels were found in 2/5 patients 1 and 5 days after surgery, respectively. The HCG levels in the CSF were elevated in 2/2 patients tested preoperatively and in 3/3 patients tested postoperatively. Five of the eight patients have been free from tumor recurrence for 0.5-2 yr. The findings show the normalization of the AFP and HCG levels in serum and CSP after treatment in all patients studied. (15 Refs) (In DAN)

34. ALPHA-FETOPROTEIN AS MARKER IN INFANTILE GERM-CELL TUMORS.

Norgaard-Pedersen B, Kamper J, Erichsen G, Hertz H, Nielsen ES, Sell A, Sogaard H, Tygstrup I, Yssing M
Klinisk kemisk afdeling, Sonderborg sygehus, DK-6400 Sonderborg, Denmark
Ugeskr Laeger; 144(18):1291-1295 1982

The serum alpha-fetoprotein (AFP) levels were determined in 19 children (11 boys and 8 girls, 5-37 mo old) with germ cell tumors. Endodermal sinus tumors (EST) of the testicles were diagnosed in seven patients, testicular teratomas in four, sacrococcygeal EST in two, sacrococcygeal EST with teratoma in four, EST and teratoma of the ovary in one and vaginal embryonal carcinoma in one. Localized disease was found in 14/19 patients, disseminated tumor disease in 5/19. Eighteen patients were subjected to surgery, 10 to chemotherapy and 9 to radiotherapy. Production of AFP was found in the seven patients with testicular EST, in six with sacrococcygeal tumors, in the patient with ovarian EST and teratoma and in the patient with vaginal embryonal carcinoma. The AFP levels, determined within the first 60 days after surgery in 18 patients, were normal in 4/18 and 80-119,000 ug/liter in 14/18. The AFP levels were determined in 14 patients beyond the first 60 days: normal values were found in 11/14. The tissue AFP levels, determined in seven patients, were elevated in five. The serum AFP levels were found to be a sensitive indicator of tumor recurrence and disease activity. Ten of the 11 patients with testicular tumors are alive without tumor recurrence, the 11th died of complication of chemotherapy. Two of the six patients with sacrococcygeal tumors are alive for more than 3 yr. One patient with ovarian tumor and another with vaginal tumor died after 1 and 2 yr, respectively. (15 Refs) (In DAN)

35. STUDIES OF THE PROGNOSTIC VALUE OF HUMAN CHORIONIC GONADOTROPIN AND ALPHA-1-FETOPROTEIN LEVELS AND HLA ANTIGENS IN MALIGNANT TESTICULAR TUMORS.

Aiginger P, Schwarz HP, Kolbe H, Kuzmits R, Kuhbock J, Mayr WR, Spona J
II. Med. Univ.-Klinik Wien, Wien, Austria
Verh Dtsch Ges Inn Med; (87):1111-1114 1981

Serum levels of human chorionic gonadotropin (HCG), alpha-1-fetoprotein (AFP), and human lymphocytic antibody (HLA) antigens were measured in 50 patients with malignant testicular tumors. Following semicastration and retroperitoneal lymphadenectomy, patients received vinblastine and bleomycin, with or without cis-platinum. Positive response to therapy correlated with normal levels of AFP; response decreased with increasing levels. No correlation between HCG levels and response could be demonstrated. High levels of HLA-A-10 and HLA-B-13 antigens were found among 40 patients. (10 Refs) (In GER)

36. ENDOCRINOPATHY ASSOCIATED WITH PINEAL TUMORS (1).

Mori K
Dept. Neurosurgery, Nagasaki Univ., Nagasaki 852, Japan
Neurol Med Chir (Tokyo); 21(4):359-363 1981

Origins, types, and hormonal production of pineal tumors are reviewed. Pineal gland tumors are broadly divided into germ cell tumors and pinealomas. Tumors with specific cell types are associated with human chorionic gonadotropin (HCG) or alpha fetoprotein production. Research on relationships between HCG-producing tumors and pubertas praecox is also discussed. (102 Refs) (In JPN)

37. ANDROBLASTOMA AND RAISED SERUM ALPHA-FETOPROTEIN WITH FAMILIAL MULTINODULAR GOITRE. CASE REPORT.

Benfield GF, Tapper-Jones L, Stout TV
Llandough Hosp., Penarth, S. Glamorgan, Wales
Br J Obstet Gynaecol; 89(4):323-326 1982

Androblastoma associated with raised levels of alpha-fetoprotein was diagnosed in a 16-yr-old girl who presented with a 10-mo history of menorrhagia and polymenorrhea after 1 yr of normal menses. A family history of multinodular goiter is discussed. A large (22 wk) pelvic mass was found at surgery to be a massive right-sided ovarian tumor with an intact capsule and weighing 1.5 kg. The strong family history of goiter was confined to the father's side, with 14 members in three generations having either clinical or histologically confirmed multinodular goiter. (12 Refs)

38. CARCINOEMBRYONIC ANTIGEN AND ENDOCRINE RESPONSE IN A PATIENT WITH SIPPLE'S SYNDROME FOLLOWING SURGERY.

Nakada T, Shigematsu H, Nagayama T, Miyauchi T, Yoshida Y, Sakiyama S, Ketayama T, Shimada F
Dept. Urology, Faculty Medicine, Toyama Medical and Pharmaceutical Univ., 2630 Sugitani, Toyama 930-01, Japan
Endocrinol Jpn; 28(5):551-562 1981

Clinical studies and serial determinations of circulating calcitonin (CT), catecholamine (CA), ACTH, and carcinoembryonic antigen (CEA) in the follow up of pre- and postsurgical period were performed in a 59-yr-old man with Sipple's syndrome. The peptides and the antigen in tissue extracts from removed adrenal pheochromocytoma (PCC), para-aortal PCC, medullary thyroid cancer (MCT), and tumor-uninvolved thyroid tissue were assayed. Substantial levels of CA and its major metabolites were present in the urine. After removal of the PCC, urinary CA and urinary vanillymandelic acid excretions gradually returned to normal levels. Each amount of CA fraction in removed PCC was much higher than that of MCT or tumor-uninvolved thyroid tissue. High levels of CEA were found prior to surgery. Significant difference was observed in the elution profile of glycoprotein extracts containing CEA from different removed tissues. Sequential determinations showed that circulating levels of CT, ACTH, and cortisol were high prior to surgery and decreased after the first surgical intervention. A marked reduction of serum CT was observed 2 wk after the second surgery (total thyroidectomy). A high amount of CT was extracted form the MCT removed both from the left and right nodules. Relatively elevated level of CT was observed in the extract of tumor-uninvolved thyroid tissue. Extracts of adrenal and ectopic PCC contained immunoreactive ACTH and beta-melanocyte stimulating hormone (beta-MSH). Beta-MSH was detected also in the right MCT and tumor-uninvolved thyroid tissue. (29 Refs)

39. BIOLOGICAL MARKERS AS AN AID IN THE CLINICAL MANAGEMENT OF PATIENTS WITH LIVER METASTASES.

Waalkes TP, Abeloff MD, Ettinger DS, Mrochek JE, Bostick WD
Johns Hopkins Oncology Center, Room 167, 600 North Wolfe St., Baltimore, MD, 21205
J Surg Oucol; 20(2):83-94 1982

Liver metastases due to the more common neoplastic diseases such as colorectal, breast, or bronchogenic carcinoma are a frequent occurrence and are associated with an ominous prognosis. Earlier detection followed by appropriate therapeutic interventions might have a decided effect on the subsequent course of disease. Controversy exists over the selection of tests with the greatest sensitivity, specificity, and potential utility. Preliminary evidence suggest that gamma-glutamyl transpeptidase and 5'-nucleotidase may be of particular significance. Four enzymes - gamma-glutamyl transpeptidase, 5'-nucleotidase, leucine aminopeptidase, and alkaline phosphatase plus carcinoembryonic antigen - were compared in the same blood samples from selected patients with breast and small cell carcinoma of the lung. Gamma-glutamyl transpeptidase was the most sensitive test with 28/29 (97%) patients with hepatic metastases having elevated enzymatic activity in their sera. For patients with small cell carcinoma of the lung followed serially, gamma-glutamyl transpeptidase activity was increased an average of 5 months before liver metastases were detected by clinical means. Two factors are important in the interpretation of the results of gamma-glutamyl transpeptidase analysis: (1) Hepatic dysfunction due to diseases other than metastatic tumor involvement can cause a rise in enzyme levels as can (2) medications or ethanol which activate the hepatic microsomal drug metabolizing system. Of particular importance, however, is the fact that antitumor chemotherapy, even intensive and multiple agent, did not appear to effect the enzyme activity in the sera of patients with breast or small cell carcinoma of the lung. Gamma-Glutamyl transpeptidase in combination with carcinoembryonic antigen may be of particular value in detecting liver metastases and in assessing subsequent response to therapy. (Author abstract) (45 Refs)

40. CLINICAL EVALUATION OF TUMOR POSITIVE IMAGING WITH I125-OR I131-LABELED ANTI-HUMAN SFP SPECIFIC ANTIBODY FOR AFP-PRODUCING TUMOR LINE (JTG-1) AND CLINICAL CASES.

Yanagisawa M, Miki M, Hirai H
Dept. Urology, Jikei Univ. Sch. Medicine, Tokyo, Japan
Nippon Hinyokika Gakkai Zasshi; 72(12):1559-1568 1981

Feasibility of imaging of specific tumors with the aid of labeled anti-human alpha-fetoprotein specific antibody (AAA) was studied in nude mice bearing the AFP-producing JTG-1 tumor and in two male patients (41 and 26 yr old) who had testicular tumors and whole body metastasis. The two patients were administered 415 uCi of the I125-labeled AAA. Whole body scanning with a PHO/CON TM-Multi-Plane Imager system was performed on days 1, 3, and 5 after injection of the AAA. Mice were given whole body scanning days 1, 3, 5 and 8 with a PHO/Gamma HP-Sciatillation Camera and pin hole collimator. Positive imaging of the tumors was achieved in 5 nude mice 5 and 8 days after administration of the I125-labeled AAA (12 uCi/mouse), but preferential localization of the labeled AAA was not observed in the two patients. Differences in imaging was thought to be due to differences in the doses of the labeled AAA and histological changes of tumors in the patients due to cis-platinum treatment. (21 Refs) (In JPN)

41. TREATMENT FOR MENINGEAL CARCINOMATOSIS IN BREAST CANCER.

Yap HY, Yap BS, Rasmussen S, Levens ME, Hortobagyi GN, Blumenschein GR

MRCP Dept. Medicine, Medical Breast Service, M.D. Anderson Hosp. and Tumor Inst., 6723 Bertner Ave., Houston, TX, 77030

Cancer; 50(2):219-222 1982

Forty breast cancer patients with meningeal carcinomatosis were treated with a combined program of whole brain irradiation therapy with intrathecal and intraventricular methotrexate and citrovorum factor rescue. Responses were seen in 26 patients (65%); 13 patients (35%) failed to respond. The median survival time for the responding patients was 6 mo, and for the nonresponders, 1 mo. Factors affecting response and survival included pretreatment spinal fluid glucose, protein, and duration of CNS-related symptomatology prior to onset of therapy. In contrast, pretreatment CSF tumor cell count, CEA and initial CNS functional status did not appear to have prognostic significance. The authors conclude that following intensive therapy there can be much improvement in the quality of life and disease-free survival in breast cancer patients with meningeal carcinomatosis. (Author abstract) (12 Refs)

42. ADJUVANT AMINOGLUTETHIMIDE THERAPY FOR POSTMENOPAUSAL PATIENTS WITH PRIMARY BREAST CANCER: PROGRESS REPORT.

Coombes RC, Chilvers C, Dowsett M, Gazet JC, Ford HT, Bettelheim R, Gordon C, Smith IE, Zava D, Powles TJ, McKinna A, White H, Henk M, Griffiths M, Bradbeer J, Neeley J, Bull JC, Topham C, Hunter-Craig I, Hale JE, Folkes A, Taylor R, Miller S, Southam JA, Tostam A, Booth RA, Gazet JC, Nash A

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Cancer Res; 42(8,Suppl):3415s-3419s 1982

A group of 122 postmenopausal patients with histologically proven node-positive primary breast cancer have been randomized to receive aminoglutethimide-hydrocortisone or placebo aminoglutethimide-placebo hydrocortisone for 2 yr. Median follow-up is 17 mo. In general treatment was well tolerated, but 15 patients required a reduction in the dose of aminoglutethimide, and of these four patients were unable to continue therapy due to side effects. Primary staging, incidence of extensive node involvement, and estrogen receptor were similar in the treatment and control arms. Dehydroepiandrosterone sulfate (DHA-S) and estrone were measured in a subgroup of patients, and significant suppression of DHA-S levels throughout the duration of the treatment period was seen in patients receiving the active drug. No significant suppression of either DHA-S or estrone levels was seen in the controls. Patients were monitored for metastases by serial liver function tests, carcinoembryonic antigen, and chest x-rays, and of 26 relapsing patients only 3 patients were not detected by this screen. We conclude that adjuvant aminoglutethimide is moderately well tolerated. It is capable of suppressing DHA-S throughout 2 yr of treatment. A further 280 patients will be entered into the study to assess the survival benefit for those taking aminoglutethimide-hydrocortisone. (Author abstract) (8 Refs)

43. CORRELATION OF SIALYLTRANSFERASE AND SIALIC ACID AND THEIR COMPARISON WITH SIX OTHER BIOCHEMICAL MARKERS FOR MONITORING THE EXTENT OF DISEASE IN PATIENTS WITH BREAST CANCER (MEETING ABSTRACT)

McDermott BJ, Quinn CC, Leamy BM, Jeffrey L, Murphy RF
Department of Biochemistry, Queen's University Belfast, Belfast, Ireland
Twenty-third Annual General Meeting of the British Association for Cancer Research, March 29-31, 1982, Edinburgh, Scotland. British Association for Cancer Research 78 pp., 1982.

Over a period of up to 24 months, post-mastectomy, the following serum markers were measured in 86 patients: carcinoembryonic antigen (CEA), C-reactive protein (CRP), alpha-acid glycoprotein (AGP), erythrocyte sedimentation rate (ESR), gamma-glutamyl transferase (gamma GT), alkaline phosphatase (AP), sialyl transferase (ST): sialic acid (SA) was determined retrospectively. Prior to therapy, there was a higher incidence of raised marker measurements in the sera of patients with metastatic cancer than in those who were apparently disease-free, except for ST. Only CEA and ST concentrations were elevated in a significantly greater number of patients with minimal disease (lymph-node involvement or recurrence) than in the tumor-free group. In those with minimal disease, 5/6 raised values were attributed to the lymph-node positive group. A patient defined as tumor-free had the most elevated ST value. Lymph-node involvement was detected clinically 6 months later. Alterations in tumor burden were reflected in 50% of the changes in ST concentrations by comparison with a correlation of greater than 75% for CEA, CRP and gamma GT measurements. ST values were raised up to 8 months before clinical detection of advancing disease in 9/17 patients. In 7 case, ST concentrations reached a peak and then declined; notably in the evolution of metastases, values returned to normal before progression was overt. ST results have been substantiated by SA estimations in both vertical and horizontal studies. (no Refs)

44. CEA: A TUMOR MARKER IN UROLOGY? (MEETING ABSTRACT).

Lymberopoulos E, Melchior H
Urologische Klinik der Stadtischen Kliniken Kassel, Kassel, W. Germany
6. Symposium fur Experimentelle Urologie, April 15-17, 1982, Bonn, W. Germany. German Association for Urology 155 pp., 1982.

The clinical value of carcinoembryonic antigen (CEA) as a tumor marker has been demonstrated principally in intestinal tumors. In a series of clinical studies it will be shown to what extent CEA is of importance as a tumor marker in urology. CEA was determined preoperatively by the enzyme immunoassay technique in a total of 45 patients with malignant tumors of the urogenital tract (17 hypernephroid carcinomas of the kidney, 12 advanced urothelial carcinomas, 9 carcinomas of the prostate, 8 malignant testicular tumors). Normal values are less than 2.5 ng/ml; the critical value as a tumor marker is reached at 5 ng/ml. As regards kidney tumors, in stage T1/T2 serum CEA levels never exceeded 5.0 ng/ml. Of 10 stage T3 tumors 2 were clearly CEA-positive; in both distant metastases were demonstrated (M1c/M1d). All urothelial carcinomas in stage T1/T2 had negative CEA reactions. Of 4 stage T3/T4 tumors, one exhibited a positive reaction in ureteral carcinoma with local invasion and invasion of the bladder as well as metastasis to the para-aortic lymph nodes. Regardless of stage carcinoma of the prostate is always CEA-negative. As for testicular tumors, no elevation of serum CEA could be found in 2 seminomas and 6 teratocarcinomas (3 shown to have metastasized to retroperitoneal lymph nodes); CEA was significantly increased in just 1 patient who had a primary retroperitoneal teratoneoplasm. CEA appears to be of no value as a tumor marker for malignancies of the urogenital tract. (no Refs) (In GER)

ULTRASTRUCTURE/ CYTOCHEMISTRY

45. GASTRIC CARCINOMA WITH ARGYROPHILIC CELLS: LIGHT MICROSCOPIC, ELECTRON MICROSCOPIC, AND IMMUNOCHEMICAL STUDY.

Prade M, Bara J, Gadenne C, Bognel C, Charpentier P, Ravazzola M, Caillou B
Histopathologie-B, Institut Gustave-Roussy, rue Camille Desmoulins, 94800 Villejuif, France
Hum Pathol; 13(6):588-592 1982

An immunochemical study of a gastric adenocarcinoma with argyrophilic cells showed two areas of tumor that react differently with the usual histochemical reagents as well as with immune sera against gastrin and mucoprotein associated with antigens. Ninety percent of the tumor cells were PAS positive and contained M2 antigen, and some also contained M1 antigen. About 30% of the M2-positive cells stained strongly with an antigastrin serum as well as with the argyrophilic reagents. The remaining 10% of tumor cells were signet-ring cells located in several clumps in the tumor. These cells were positive for both PAS and alcian blue and contained intestinal M3 antigen. Forty-five percent of them also contained M1 gastric antigens. Carcinoembryonic antigen (CEA) was found in the cytoplasm of each tumor cell. The presence of CEA and M1 antigen together indicates a fetal pattern, suggesting that the cells originate from very immature gastrointestinal stem cells. (Author abstract) (16 Refs)

46. IMMUNOHISTOCHEMICAL DETERMINATION OF THE CARCINOEMBRYONIC ANTIGEN IN CARCINOMA OF THE COLON.

de Beveraggi MT, Caccamo D
Servicio de Patologia, Hospital Italiano, Buenos Aires 1181, Argentina
Medicina (B Aires); 42(2):115-121 1982

Sixty patients bearing adenocarcinoma of the large bowel were evaluated immunohistochemically for the presence of the carcinoembryonic antigen (CEA) in the tumor and in the regional lymph nodes. The immunoperoxidase technique was utilized in the study of surgically resected specimens. A clear correlation was found between the amount of CEA present and the survival of the patient. Thus of the patients in the most advanced category (Dukes C), 66% of those with minimal CEA survived an av of 37 mo, 53% of those with medium amounts of CEA survived an av of 35 mo, and no patient with maximal amounts of CEA survived for more than an av of 9 mo. Survival to 18 mo for each category equaled 9/10, 11/14 and 1/10, respectively.Prognostic value of this technique was emphasized. (17 Refs) (In SPA)

47. ARGYROPHIL CELLS IN EARLY GASTRIC CARCINOMA: AN IMMUNOHISTOCHEMICAL AND ULTRASTRUCTURAL STUDY.

Tahara E, Ito H, Shimamoto F, Taniyama K, Iwamoto T, Sumiyoshi H, Kajihara H, Yamamoto M
First Dept. Pathology, Hiroshima Univ. Sch. Medicine, 1-2-3 Kasumi, Minami-ku, Hiroshima 734, Japan
J Cancer Res Clin Oncol; 103(2):187-202 1982

Eighteen argyrophil cell carcinomas in 101 early gastric carcinomas were examined histologically, ultrastructurally, and immunohistochemically for polypeptides, carcinoembryonic antigen (CEA), lysozyme, and human chorionic gonadotrophin (hCG). Seven of these 18 tumors had gastrin, and 2 of 7 tumors also contained somatostatin. In all of these 18 tumors CEA were demonstrated. Seven had lysozyme and 5 of 7 tumors also contained gastrin; hCG were present in 4 of 18 tumors and 2 of 4 tumors had gastrin, CEA, mucin, and lysozyme simultaneously. Argentaffin cells were found in 7 of 18 tumors. Of the above seven tumors containing gastrin, three had argentaffin cells. Ultrastructurally, several types of secretory granules were noted and tumor cells resembling D1-or P cells were present in 9 of the 18 tumors. Macroscopically, many of the tumors showed IIc or IIc + III type. Histologically, the 18 tumors consisted of 6 well differentiated adenocarcinomas and 12 poorly differentiated adenocarcinomas including signet-ring cell carcinoma. These 12 tumors frequently developed in the stomach of young females. In view of our previous investigation, it was suggested that the IIc-type argyrophil cell carcinoma histologically showing poorly differentiated adenocarcinoma may be related to scirrhous carcinoma of the stomach. (Author abstract) (30 Refs)

48. LARGE-BOWEL CARCINOMAS WITH DIFFERENT PLOIDY, RELATED TO SECRETORY COMPONENT, IGA, AND CEA IN EPITHELIUM AND PLASMA.

Rognum TO, Thorud E, Elgjo K, Brandtzaeg P, Orjasaeter H, Nygaard K
Histochemical Lab., Inst. Pathology, Natl. Hosp., Rikshospitalet, Oslo, Norway
Br J Cancer; 45(6):921-934 1982

Immunofluorescence staining for carcinoembryonic antigen (CEA), secretory component (SC), and epithelial IgA was evaluated semiquantitatively in 85 large-bowel carcinomas in relation to degree of tumor differentiation, Dukes' stage, and plasma CEA level. The tumors were divided into a near-diploid (ND, 28) and an aneuploid group (AN, 57) by means of flow-cytometric DNA measurements. Expression of SC and IgA in neoplastic epithelium was positively related to differentiation in both groups. The AN tumors scored significantly higher for CEA than the ND ones, but the staining was apparently unrelated to differentiation or Dukes' stage. CEA expression in the transitional mucosa adjacent to ND tumors was negatively correlated with tumor differentiation, whereas epithelial IgA and SC in this zone showed a substantially higher positive correlation with tumor differentiation, and a somewhat stronger negative correlation with Dukes' stage in the ND than in the AN group. Plasma CEA levels were significantly related to Dukes' stage, only in patients with AN tumors, and only in this group were positively correlated with estimates of total tumor CEA for Dukes' Stages A and B. For Dukes' Stages C and D (disseminated tumors), moreover, the plasma CEA levels were found to be significantly higher in the AN group. These findings indicate that the DNA profile of large-bowel carcinomas is related both to the way neoplastic cells influence the activity of the transitional mucosa and their capacity for expression and release of epithelial products. AN tumors thus seem to be more active as 'secretors' of CEA than ND ones. (Author abstract) (51 Refs)

49. CARCINOEMBRYONIC ANTIGEN (CEA) IN BONE-MARROW METASTASES.

Bezares RF, Cavagnaro FJ, Palmer LR, Diaz AE, Domenichini E
Hospital Minicipal 'T. Alvarez', Donato Alvarez 3411, 1431 Buenos Aires, Argentina
Sangre (Barc); 27(1):7-14 1982

Twenty-two bone-marrow biopsy samples were examined, 11 of them having metastases from epithelial neoplasms. CEA immunolabeling was positive in five of six cases of adenocarcinoma (83%), with stronger intensity for the digestive tract tumors. Weak-positive or negative results were found in the cases with anaplasia and intense dedifferentiation which showed trabecular or infiltrative histologic patterns. The technique is feasible for bone-marrow biopsy specimens in spite of the routine treatment to which such samples are subjected. (Author abstract) (18 Refs) (In SPA)

50. IMMUNOPEROXIDASE STAINING OF CARCINOEMBRYONIC ANTIGEN WITH MONOCLONAL ANTIBODIES IN ADENOCARCINOMA OF THE COLON.

Lindgren J, Wahlstrom T, Bang B, Hurme M, Makela O
(c/o Wahlstrom) Dept. Pathology, Univ. Helsinki, Haartmaninkatu 3, SF-00290 Helsinki 29, Finland
Histochemistry; 74(2):223-227 1982

Application of monoclonal antibodies to the immunoperoxidase staining of carcinoembryonic antigen (CEA) is described. A distinct positive staining of the neoplastic epithelial cells was seen in all sections stained with unadsorbed anti-CEA ascites fluids and the rabbit anti-CEA-antiserum. All controls including the ascites fluids adsorbed with purified CEA were negative. The nonspecific background staining of the ascites fluids was negligible in all dilutions used giving a better distinction than the rabbit antiserum. (9 Refs)

51. ELASTOSIS AND IMMUNOCYTOCHEMICAL STUDY. TWO NEW FACTORS FOR THE HISTOPATHOLOGICAL PROGNOSIS OF BREAST CANCER.

Bogomoletz W
Institut Jean-Godinot, Reims, France
Rev Med Brux; 3(3):147-150 1982

The presence of elastosis and the immunocytochemical detection of carcinoembryonic antigen (CEA) are discussed as prognostic indicators for breast cancer (BC). Abundant elastosis has been described in the two most common forms of invasive BC, cannular and lobular BC. Elastosis in BC may be localized or diffuse. Mesenchymal cells, particularly fibroblast and muscle fibers, appear to be the source of elastin synthesis. A significant correlation exists between elevated levels of elastosis and longer postoperative survival in BC patients. A correlation also exists between high levels of elastosis and Grade I tumors. Receptor-positive tumors seem to contain greater elastosis. Studies using immunoperoxidase technics have shown that 50-80% of BC are positive for CEA. Positivity of BC cells for CEA does not seem to be related to histological type of the tumor but possibly is associated with the degree of cellular differentiation. CEA-positive BC and the presence of lymphatic metastases show a strong correlation. (22 Refs) (In FRE)

52. EXPRESSION OF DR ANTIGENS IN FRESHLY FROZEN HUMAN TUMORS.

Thompson JJ, Herlyn MF, Elder DE, Clark WH, Steplewski Z, Koprowski H
Div. Surgical Pathology, Hosp. Univ. Pennsylvania, Box 527, 3400 Spruce St., Philadelphia, PA, 19104
Hybridoma; 1(2):161-168 1982

Using frozen tissue sections, a monoclonal antibody (WI 691-13-17) known to detect an epitope common to all DR antigens on the beta (light) chain of DR antigens, and a two-step indirect immunoperoxidase technique, DR antigens were found on all metastatic lesions tested and on many primary tumors and their histogenetic precursors. In all, 106 benign and malignant tumors and 255 normal tissues were tested. All metastatic and most of the primary tumors apparently expressed DR antigens; malignancies derived from ectodermal, endodermal, and mesodermal embryonic layers all showed DR expression. DR antigen expression was seen in all lesions of the melanocytic neoplastic system as defined by Elder and co-workers, with precursor lesions demonstrating relatively few positive cells, primary and metastatic lesions progressively more. A subpopulation of lymphocytes, macrophages, endothelial cells, and Langerhans cells also exhibited DR antigen expression. The quantitative intensity of staining among the cells of the lesions tested ranged from negative to variable amounts. This technique allows individual cells to be assessed for antigen expression and presumably more accurately reflects in vivo antigen expression than results obtained from cells selected by tissue culture methods. (13 Refs)

53. IMMUNE HISTOCHEMICAL DEMONSTRATION OF TUMOR-ASSOCIATED ANTIGENS IN TESTICULAR GERM-CELL TUMORS.

Jacobsen GK, Jacobsen M, Clausen PP
Patologisk-anatomisk institut, Kobenhavns amts sygehus i Herley, DK-2730 Herlev, Denmark
Ugeskr Laeger; 144(18):1300-1303 1982

Fifty-eight consecutive testicular germ-cell tumors were investigated for the presence of alpha-fetoprotein (AFP) and human chorionic gonadotropin (HCG) by the indirect immune peroxidase technique. Pure seminoma was diagnosed in 25/58 patients, embryonal carcinoma (EC) in 4, yolk sac tumor (YST) in 1, teratoma in 3, EC with seminomatous component in 5, EC with YST component in 1, EC with teratoma in 1, YST with teratomatous component in 2, EC with YST and teratomatous components in 6, YST with teratomatous and seminomatous components in 2, YST with choriocarcinoma in 2, EC with YST and seminomatous components in 3 and EC with YST, teratomatous and choriocarcinomatous components in 1. AFP was detected in 0/37 seminomatous components, 12/21 embryonal carcinoma components, 18/18 YST components, and 9/22 teratomatous components. HCG was detected in 3/3 choriocarcinoma components, 10/10 nonseminomatous components with syncytial giant cells, 1/1 seminoma with syncytial giant cells and 1/2 seminomas with tumor giant cells. No morphological difference was found between AFP-positive and AFP-negative embryonal carcinomas (AFP was present in 12/21 embryonal carcinomas). AFP was demonstrated in all types of yolk sac structures. HCG was demonstrated partly in the syncytiotrophoblasts of chorionic carcinoma components and in syncytial giant cells in 2 seminomas and 10 nonseminomatous tumors. Neither AFP nor HCG were demonstrated in the actual tumor tissue in seminomas or in components of seminomas. (9 Refs) (In DAN)

REVIEWS/ OTHER RELATED STUDIES

54. THE PREDICTIVE VALUE OF DIAGNOSTIC MEASURES.

Kobberling J
Medizinische Klinik und Poliklinik, Universitat Gottingen, Robert-Koch-Str. 40, D-3400 Gottingen, W. Germany
Dtsch Med Wochenschr; 107(15):591-595 1982

The predictive value of a diagnostic test is directly related to the prevalence of the disease the test is designed to detect. As illustrations the human lymphocyte antibody B27 test for Bechterew's disease, the general feeling test for influenza, the glucose tolerance test for late diabetes mellitus, newborn screening tests for phenylketonuria and primary hyperthyroidism, and carcinoembryonic antigen tests for detection of tumor diseases are discussed. The sensitivity and specificity of such tests are improved by proper targeting of the tests to appropriate patients. (8 Refs) (In GER)

55. BIOCHEMICAL MARKERS.

Higashino K, Sumikawa K
Third Dept. Internal Medicine, Osaka Univ. Sch. Medicine, Osaka, Japan
Nippon Rinsho; 40(1):43-50 1982

Biochemical markers used in diagnosing hepatic, bile duct, pancreatic, and other types of cancer are discussed. The common markers used in detecting cancer include C-reactive protein, glutamic oxaloacetic transaminase, glutamic pyruvic transaminase, lactate dehydrogenase (LDH), LDH4, LDH5, cholesterol, and serum amylase. Markers used to detect liver cancer include alpha-fetoprotein, alkaline phosphatase isoenzyme, gamma-guanosine triphosphate isoenzyme, ferritin, aldolase isoenzyme, 5'-nucleotidylphosphorodiesterase isoenzyme, and other newly discovered chemicals. Markers used to detect cancer of the bile duct or to distinguish cancerous from benign tumors include fetoprotein and alpha-antitrypsin. Markers for pancreatic cancer include pancreatic oncofetal antigen, carcino-embryonic antigen, ribonuclease, galactosyltransferase isoenzyme, and other chemicals. (44 Refs) (In JPN)

56. IMMUNOLOGICAL MARKERS.

Matsuno S, Kobari M, Kodera T, Sato T
First Dept. Surgery, Tohoku Univ. Sch. Medicine, Sendai, Japan
Nippon Rinsho; 40(1):51-57 1982

Diagnostic significance of alpha-fetoprotein (AFP), carcinoembryonic antigen (CEA), immunosuppressive acidic protein (IAP), pancreatic oncofetal antigen (POA), basic fetoprotein (BFP), and ferritin (F) as tumor markers for hepatic, choledochal, and pancreatic cancer is discussed. AFP and POA are considered to be particularly good markers for liver cancer and pancreatic cancer, respectively, due to the particular characteristics of the organs themselves and the high frequency of the presence of such markers associated with tumors. However, use of these markers alone is not sufficient for early detection of the tumors, so combination assays must be performed. Combining measurements of AFP, BFP, and F for liver cancer, BFP, IAP, and CEA for choledochal cancer, and AFP, BFP, IAP, CEA, and POA for pancreatic cancer was suggested, in conjunction with the leukocyte adherence test, to improve immunological diagnosis of cancer. (23 Refs) (In JPN)

57. BIOCHEMICAL MARKERS FOR CANCER.

Chu TM
Dept. Diagnostic Immunology Res. and Biochemistry, Roswell Park Memorial Inst., Buffalo, NY
Clin Biochem Anal; 11:375pp. 1982

Selected topics on biochemical markers, which have been utilized in clinical oncology, are presented and a possible approach to the study of the basic mechanism of the marker at the molecular level is described. Topics related to biochemical markers are discussed under the following headings: immunological approach to the biochemical markers for cancer, alpha fetoprotein, carcinoembryonic antigen as a tumor marker, enzymes as tumor markers, developmental alkaline phosphatases as biochemical tumor markers, prostatic acid phosphatase in human prostate cancer, biochemical markers for the differential diagnosis of leukemias, steroid-receptor interactions in normal and neoplastic mammary tissues, alteration and clinical significance of alteration of isoferritins in human malignancy, polyamines as biochemical markers of tumor growth parameters, ectopic hormone production by tumors, immunoglobulins as cancer markers in humans, multiple markers in the management of cancer patients, protein markers for androgenic activity in rat ventral prostate. (1283 Refs)

58. TUMOR MARKERS.

Ewing HP, Newsom BD, Hardy JD
Dept. Surgery, Univ. Mississippi Sch. Medicine, Jackson, MS
Curr Probl Surg; 19(2):53-94 1982

Oncofetal tumor markers, other oncofetal antigens, placental proteins and hormones, ectopic hormones, lactation-associated protein markers, tumor markers produced in response to neoplasia, and multiple tumor marker screening are discussed focusing on clinical and surgical aspects of interest. Association of alpha-fetoprotein (AFP) not only with hepatoma, but also with tumors of germ cell origin and less frequently with carcinomas of the stomach is confirmed. AFP may be detected by a number of assay techniques, which vary in sensitivity. Carcinoembryonic antigen (CEA) assays are used in screening for malignancy, assesssing prognosis, detection of recurrent carcinoma, and monitoring response to therapy. Cigarette smoking is the most common reason for an elevated CEA titer in a patient without carcinoma. Association of colorectal carcinoma and elevated CEA titers have been confirmed in 80-97% of patients. Clear conclusions concerning the nature and clinical usefulness of fetal sulfoglycoprotein, pancreatic oncofetal antigen, and additional fetal antigens cannot presently be made. Neoplasms associated with human chorionic gonadotropin (HCG) are listed. The clinical usefulness of serial determination of nonectopic HCG has been well established. Criteria for establishment of ectopic hormone secretion and hormonal tumor markers associated with carcinoma of the lung are presented. Tumor markers produced in response to neoplasia are polyamines, nucleosides and nucleotides, and hydroxyproline. Many tumors may produce multiple markers. (213 Refs)

59. GASTROINTESTINAL CANCER 1.

DeCosse JJ, Sherlock P
Memorial Sloan-Kettering Cancer Center, New York, NY
Gastrointestinal Cancer 1. The Hague, Martinus Nijhoff Publishers, Cancer Treatment and Research, Vol. 3, 452 pp., 1981.

The biology of gastrointestinal neoplasia (GN) and contemporary principles for current diagnosis and management of GN are presented. Topics include cell kinetics of GN and its precursor states; genetic aspects of gut cancer; systemic manifestations of gut malignancy; epidemiology and early detection of cancer of the esophagus; epidemiology of gastric cancer and its precursor lesions; early detection of gastric cancer; cancer of the gastric stump; metabolic epidemiology of large bowel cancer; colonoscopy in the prevention, detection, and treatment of large bowel cancer; cancer in inflammatory bowel disease; role of carcinoembryonic antigen in large bowel cancer; lymphomas of the gut; functioning tumors of the gut; epidemiology, early diagnosis, and treatment of liver cell cancer; and chemotherapy of pancreatic, colorectal, and gastric cancer. (1781 Refs)

60. ROLE OF CEA IN LARGE BOWEL CANCER.

Colacchio TA, Logerfo P
Columbia-Presbyterian Medical Center, New York, NY, 10032
Gastrointestinal Cancer 1. Decosse JJand Sherlock P, ed. The Hague, Martinus Nijhoff Publishers, Cancer Treatment and Research, Vol. 3, 452 pp., 1981.

The role of carcinoembryonic antigens (CEA) in management of large bowel cancer, and their importance in determination of recurrence, are reviewed. Topics include CEA-substance, CEA in non-malignant tissues, serum levels of CEA in patients without malignancy, CEA in malignant disorders, CEA in large bowel cancer (screening, prognosis, marker for recurrence, CEA and second-look operations, identification of high-risk groups, monitoring response to therapy), and other applications of CEA. (52 Refs)

61. CURRENT PROBLEMS IN CANCER: TESTICULAR CARCINOMA.

Paulson DF
Dept. Urologic Surgery, Duke Univ. Medical Center, Durham, NC
Curr Probl Cancer 6(11): 44 pp., 1982.

Testicular tumors, while rare (1% of all male cancers for an annual incidence of 2.3/100,000), are of major clinical significance since they occur in young men and are biologically aggressive. The various histologic patterns of testicular cancer are described. These include seminoma, embryonal carcinoma, teratoma, and choriocarcinoma. Classically the young male presents with a painless scrotal mass. Between 6 and 21% of patients with testicular tumors have an associated antecedent history of trauma. Trauma probably initiates self-examination and subsequent discovery of an otherwise occult mass. Male patients should be examined both erect and supine with special attention directed to scrotal contents. The differential diagnosis of the scrotal mass should include epididymitis, epididymo-orchitis, hydrocele, inguinal hernia, hematocele, hematoma, torsion, spermatocele, varicocele, and gumma. It is wise to consider malignancy where diagnosis is in question. Treatment selection, biological marker proteins, staging, and clinical management are discussed. (97 Refs)

62. PROSPECTS IN LARGE BOWEL CANCER.

de Jode LR
Section Proctology, Royal Society Medicine, London, England
J R Soc Med; 75(5):301-303 1982

Detection, diagnosis, treatment, and prognosis for patients with large bowel cancer are reviewed. Patients with premalignant conditions should be identified and treated, with emphasis on extirpation of adenomas. Detection and treatment of early carcinomas (Duke Stage A) can result in 90% 5-yr survival. The mainstay of treatment of large bowel cancer remains adequate cancer surgery. Thorough bowel preparation and meticulous attention to detail are vital to safe anastomosis. Before considering laparotomy, disseminated disease and other causes of elevated carcinoembryonic antigen must be excluded as far as possible; the possibility of metachronous carcinoma should be kept in mind. (22 Refs)

63. TUMOR MARKERS IN GERM-CELL TUMORS, CLINICAL APPLICATIONS AND RESEARCH ASPECTS.

Clausen PP, Norgaard-Pedersen B, Arends J, Ingild A, Jacobsen GK, Jacobsen M, Juhl BR, Kjaersgaard E, Nissen MH, Schultz-Larsen P, Toftager-Larsen K, Zeuthen J
Patologisk avdeling, kommunes Hvidovre hospital, Hvidovre, Denmark
Ugeskr Laeger; 144(18):1285-1290 1982

A review of tumor markers in patients with germinal cell tumors shows that alpha-fetoprotein (AFP) and human chorionic gonadotropin (HCG) have attained diagnostic significance in recent yr. Elevated AFP levels are found in sera of patients with yolk sac tumors, while the HCG levels are raised in patients with choriocarcinoma. The tumor markers are determined preoperatively in connection with diagnostic functional classification of the tumors and also postoperatively for therapy control. (84 Refs) (In DAN)

64. INHIBITION OF TUMOR INDUCTION AND DEVELOPMENT.

Zedeck MS, Lipkin M
Memorial Sloan-Kettering Cancer Center, New York, NY
Inhibition of Tumor Induction and Development. New York, Plenum Press, 233 pp., 1981.

Major aspects of chemoprevention, focusing on the inhibition of carcinogen formation, absorption, and metabolic activation and interaction with cell macromolecules, as well as prevention through immunological approaches, are outlined. Inhibition of chemical carcinogenesis by phenols, coumarins, aromatic isothiocyanates, flavones, and indoles and inhibition of carcinogen metabolisms and action by disulfiram, pyrazole, and related compounds are discussed. Retinoids and chemoprevention of cancer; ascorbic acid inhibition of N-nitroso compound formation in chemical, food, and biological systems; alpha-tocopherol and its relationship to tumor induction and development; trace elements and metals as anticarcinogens; and the protective role of plant sterols in chemical carcinogenesis are described. Immunoprevention is discussed with respect to detection of tumor-associated antigens in experimental rat bowel carcinomas, evidence that embryonic antigens are associated with bowel carcinomas, enhanced 1,2-dimethylhydrazine (DMH)-induced tumorigenesis in imunosuppressed rats, inhibitory effect on bowel carcinogenesis by immunization with transplantable syngeneic colon carcinoma and by immunization with fetal tissue, inhibition of DMH-induced carcinogenesis in multiparous rats, effects of tumor resection on the development of additional primary tumors, and regression of early primary bowel carcinomas by multimodal immunological treatment are discussed. (738 Refs)

65. MOLECULAR MECHANISM OF EXTINCTION OF LIVER-SPECIFIC FUNCTIONS IN MOUSE HEPATOMA X RAT FIBROBLAST HYBRIDS: EXTINCTION OF THE ALBUMIN GENE.

Papaconstantinou J, Wong E, Ratrie H, Szpirer C, Szpirer J
Div. Cell Biology, Dept. Human Biological Chemistry and Genetics, Univ. Texas Medical Branch, Galveston, TX, 77550
Somatic Cell Genet; 8(3):363-376 1982

The presence of mouse and rat albumin genes in the mouse x rat hybrid cells is demonstrated, and the extinction of albumin synthesis is shown to be possibly due to the virtual absence of cytoplasmic albumin messenger (m) RNA. The presence and activity of the beta-glucuronidase gene, which is located on mouse chromosome 5, as are the albumin and alpha-fetoprotein (AFP) genes, was established in BJ hybrids (of mouse hepatoma line BWTG3 and rat fibroblast line JF1). Southern blot analyses yielded direct evidence for the presence of the mouse and rat albumin DNA sequences in the hybrids. Reassociation data indicate that there are less than 11 albumin mRNA molecules/cell in the BJ hybrids, but that the parent BWTGE has about 10,900 mRNA molecules/cell; extinction of albumin production is thus related to the greater than 1,000-fold reduction of the mRNA level. That the mechanism of extinction of albumin production acts specifically and most probably involves an inhibition of transcription reinforces the idea that this mechanism is similar to those which in normal development block the expression of fibroblast albumin and AFP genes. (56 Refs)

66. MALIGNANT TRANSFORMATION OF HUMAN EMBRYO RETINOBLASTS BY CLONED ADENOVIRUS 12 DNA.

Byrd P, Brown KW, Gallimore PH
Cancer Res. Campaign Laboratories, Dept. Cancer Studies, Medical Sch., Univ. Birmingham, Birmingham B15 2TJ, England
Nature; 298(5869):69-71 1982

Isolation of a recombinant plasmid (pAsc2)-trans human embryo retinoblast (HER) cell line that contains many copies of the adenovirus Type 12 (Ad 12) transforming region, expresses virus-specified proteins, and following inoculation into athymic mice, forms tumors which resemble retinoblastomas is described. Primary cultures of human retinoblasts were transfected with pAsc2, and one transformed focus, identified 45 days after transfection, was isolated and established as a continuous cell line. The cell line has been designated Ad 12 HER1 and was the first reported Ad 12-transformed human cell line. Cytogenetic analysis revealed a pseudotetraploid human karyotype. The Ad 12 HER1 cell line was grown beyond the thirty-sixth tissue culture passage level and at no time has its growth entered a crisis phase. When Ad 12 HER1 cell DNA was digested with the restriction endonucleases BglII or SstI and subjected to Southern blotting analysis using P-labeled Ad 12 EcoRI-C DNA fragments as a probe, Ad 12 sequences were found on many DNA fragments whose sizes ranged from greater than 12 kilobase pairs (kb) to 2.2 kb. As these enzymes cleave host DNA sequences only, each fragment represented a separate insert of pAsc2 sequences. Results suggested that Ad 12 HER1 cells contain intact, integrated copies of viral and vector sequences and it is likely that some of the inserts contain tandem repeats of the entire recombinant plasmid. Histological analysis of the Ad 12 HER1-induced tumors showed them to consist of clusters of small cells with many mitotic figures characteristic of poorly differentiated human retinoblastomas. (29 Refs)

67. THE VALUE OF COMPUTER TOMOGRAPHY IN THE DIAGNOSIS OF LOCAL RECURRENCES OF CARCINOMA OF THE RECTUM.

Klose KJ, Duber C, Kempf P, Gunther R, Schweden F
Institut fur Klinische Strahlenkunde, Johannes-Gutenberg-Universitat, Langenbeckstrasse 1, D-6500 Mainz 1, W. Germany
ROEFO; 136(5):538-542 1982

The tendency of rectal carcinomas to recur makes it necessary to re-examine these patients repeatedly. The tissues remaining following resection of the rectum can only be examined directly by computer tomography. The value of this procedure in the diagnosis of local recurrences has so far not been established. The results of computer tomography must therefore be correlated with already established methods, particularly clinical examination and CEA measurements. (Author abstract) (44 Refs) (In GER)

68. TRANSCATHETER ARTERIAL EMBOLIZATION THERAPY.

Yamada R, Nakamura K

Dept. Radiology, Wakayama Prefectural Medical Coll., Wakayama, Japan

Nippon Rinsho; 40(1):183-190 1982

Appropriate circumstances to use embolization, the method of transcatheter arterial embolization, methods to evaluate embolization, complications and side effects of embolization, and results of treating patients with embolization are discussed. Six-mo, 1-yr, and 2-yr actuarial survival rates of 60 patients who were treated with embolization for unresectable hepatocellular cancer were 61%, 42.7%, and 30.2%, respectively. Evaluation of the embolization is performed by angiography, measuring postoperative serum alpha-fetoprotein levels, and enhanced whole body computed tomography scans. Primary complications of the embolization were fever (97%), abdominal pain (60%), and abdominal discomfort (35%). The fever was well controlled with antipyretics and steroids within 10 days. Four patients died within 1 mo of surgery due to hepatic insufficiency, but all of these patients had tumor emboli in the main segment of the portal vein. (15 Refs) (In JPN)

69. RETROPERITONEAL TUMORS (RPT): REPORT OF 10 CASES (MEETING ABSTRACT).

Rubben H, Hannappel J, Ammon J, Lutzeyer W

Abt. Urologie und Radiologie der RWTH Aachen, Goethestr 27/29, 5100 Aachen, W. Germany

28 Tagung der Nordrhein-Westfalischen Gesellschaft fur Urologie, May 6-8, 1982, Krefeld, W Germany Nordrhein-Westfalischen Gesellschaft fur Urologie; 1982

According to definition retroperitoneal tumors (RPT) comprise just neoplasms of the retroperitoneum which are neither attached to an organ nor arise as lymph node or distant metastases of other primary tumors. The 10 cases here described and initially treated between 1974 and 1981 consist of 2 seminomas (without testicular tumor), 2 dedifferentiated carcinomas of uncertain origin, 1 leiomyosarcoma, 1 reticulum cell sarcoma, 1 fibrous xanthoma, 1 malignant lymphoma, 1 fibrosarcoma and 1 liposarcoma. The symptomatology was essentially uncharacteristic (unclear abdominal ailments, weight loss, impaired performance, palpable tumor). Diagnosis should first exclude a primary non-RPT (clinical examination, especially of the testes, excretory urography, barium enema, gastrointestinal passage). Local tumor extension and an attempt at diagnosing the type can be documented by sonography, computer tomography, angiographic procedures, determinations of vanilmandelic acid, beta human chorionic gonadotropin and alpha-fetoprotein titers. Before planning treatment distant metastases should be sought out by chest x-ray, whole body bone scan, and liver sonography. The basis for therapy is primary tumor reduction through irradiation and chemotherapy and an attempt at radical tumor removal through surgery. Because of the usually advanced tumor stage, however, the prognosis, with the exception of seminomas is poor. (no Refs) (In GER)

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ONCOFETAL PROTEINS

SERIES CB01 No. 82/12

DECEMBER, 1982

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STRUCTURE/ IDENTIFICATION/ CHARACTERIZATION

1. IDENTIFICATION OF CARCINOEMBRYONIC ANTIGEN (CEA) IN BILE OF PATIENTS WITH MALIGNANT BILIARY TRACT DISEASE.

Konomi K, Nakamura K, Tobimatsu M, Saito S, Toyoda K, Yasunami Y

Dept. Surgery I, Kyushi Univ., Faculty Medicine, 3-1-1 Maidashi, Higashi-ku, Fukuoka 812, Japan

Jpn J Surg; 12(3):184-190 1982

Diagnostic efficacy of determination of bile levels of carcinoembryonic antigen (CEA) was studied in 12 patients with cholelithiasis (6 men, 6 women; 32-77 yr old); 19 with liver, bile duct, or gallbladder cancer (9 men, 10 women; 45-77 yr old); and 7 with cancer of the head of the pancreas or the duodenal ampulla (6 men, 1 woman; 38-69 yr old). Bile samples were obtained from biliary tract drainage (the av period of sampling after drainage was 14.7-22.3 days in patients with benign lesions, 19.4 days in patients with hepatobiliary neoplasms, and 33.4 days in patients with cancer of the head of pancreas or duodenal ampulla). The av CEA levels in the bile

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from the patients with benign lesions, hepatobiliary neoplasms, and cancer of the head of the pancreas or duodenal ampulla were 13.1, 7.6, and 8.8 nanog/ml, respectively. The corresponding serum CEA levels were 2.0, 3.3, and 2.5 nanog/ml. It was concluded that determination of bile CEA levels is more useful in differential diagnosis of hepatobiliary neoplasms than serum CEA levels. (19 Refs)

2. MESOTHELIOMA: PROFILE OF KERATIN PROTEINS AND CARCINOEMBRYONIC ANTIGEN. AN IMMUNOPEROXIDASE STUDY OF 20 CASES AND COMPARISON WITH PULMONARY ADENOCARCINOMAS.

Corson JM, Pinkus GS
Dept. Pathology, Brigham and Women's Hosp., 75 Francis St., Boston, MA, 02115
Am J Pathol; 108(1):80-88 1982

The distribution of keratin proteins and carcinoembryonic antigen (CEA) in 20 diffuse pleural malignant mesotheliomas and 20 adenocarcinomas of the lung was determined with the use of an indirect immunoperoxidase method. Keratin proteins were identified in all of the mesotheliomas, with strong staining observed in 17 of the cases. Tumor cells of various histologic types (tubular, papillary, solid, and spindle) revealed staining for keratin proteins. A variety of staining patterns were observed, but the homogeneous pattern predominated, in either a diffuse (16 cases) or focal form (4 cases). CEA was usually absent (11 cases), but weak or equivocal staining was also observed (8 cases), and 1 case uniquely exhibited moderate staining for CEA. In contrast, adenocarcinomas of the lung usually stained weakly or negatively (18 cases) for keratin proteins and exhibited a predominantly peripheral staining pattern. All cases, however, stained strongly or moderately for CEA. The profile of strong keratin staining and weak or absent CEA staining appears characteristic of mesotheliomas and may be diagnostically useful in defining the epithelial element of these neoplasms and in distinguishing them from adenocarcinomas. (Author abstract) (17 Refs)

3. IDENTIFICATION OF AN ONCOFETAL ANTIGEN (GP90) ON MURINE B16 MELANOMA CELLS.

Nishio C, Ishii Y, Ishii K, Kikuchi K
(c/o Ishii) Dept. Pathology, Sapporo Medical Coll., S1 W17, Sapporo 060, Japan
Eur J Cancer Clin Oncol; 18(6):579-588 1982

A xenoantiserum to murine B16 melanoma cells was developed by immunizing rabbits with cultured B16 melanoma cells. This antiserum could, after extensive absorption with normal C57BL/6 mouse tissues, react with syngeneic (B16) and allogeneic (HP) melanomas as well as with other murine neoplasms, including syngeneic 75S adenocarcinoma, allogeneic myeloma and leukemic T cell lines. The antiserum also cross-reacted with syngeneic fetal fibroblasts and with an allogeneic fetal fibroblast cell line (SC-1) either uninfected or infected with murine leukemia virus (MuLV). Immunoprecipitated material from B16 melanoma cell-surface glycoproteins that had been labeled with [125I] by lactoperoxidase and purified by a Lentil lectin column was analyzed by one-dimensional SDS- and two-dimensional polyacrylamide gel electrophoresis, which disclosed an acidic glycoprotein with a molecular weight (mol wt) of 90 K daltons. Absorption studies suggested that the 90 K mol wt glycoprotein represented the oncofetal moiety expressed in murine melanoma, carcinoma and fetal tissues. When the amount of this antigen in developing C57BL/6 mouse fetuses was measured by absorption assays, we found that it was expressed strongly in those fetuses just before birth. Binding and absorption studies demonstrated that the 90 K mol wt glycoprotein, while being expressed on a variety of fetal and neoplastic cells in mice, did not exist at detectable levels in normal tissues of adult C57BL/6 mice, including tissues of the thymus, lymph node, spleen, liver, brain, lung and kidney. (Author abstract) (26 Refs)

4. HISTOCHEMICAL LOCALIZATION OF A NEW TUMOR-ASSOCIATED ANTIGEN (MEETING ABSTRACT).

Ramsey R, Lovins R, Hokama Y
Lancer, Division of Sherwood Medical, Foster City, CA, 94404
Fed Proc; 41(3):555 1982

Tumor-Associated Antigen (TAG) is a glycoprotein of 50,000-60,000 molecular weight which can be found in carcinomatous tissue. Tissue sections were examined using fluorescently-labelled antibody to TAG. Direct immunofluorescent staining was also carried out using anti-CEA (carcinoembryonic antigen) serum. Adenocarcinomas from the following primary sites were studied: Colon-rectum, 15; stomach, 5; breast, 6; and ovaries, 2. Examination of the sections stained with labelled antibody demonstrated that the primary staining of the malignant tissue was associated with cell plasma membranes. Cytoplasmic staining was also observed in certain tumors. No appreciable staining of the inflammatory or necrotic tissue around lesions was observed. Faint membrane staining was associated with some of the normal tissues studied. The staining observed with tumor tissue using fluorescently labelled anti-CEA was similar to the pattern already described for anti-TAG in that the anti-CEA staining was mainly of cell membrane of the tumor cells. Cross-inhibition studies demonstrated that unlabelled anti-CEA serum did not inhibit staining for TAG by fluorescently-labelled anti-TAG serum. Conversely, unlabelled anti-TAG serum did not inhibit the staining by the labelled anti-CEA serum, indicating that the two antigens possess distinct immunochemical specificities. (no Refs)

5. IDENTIFICATION AND DIFFERENTIATION OF CARCINOEMBRYONIC ANTIGEN DETERMINANTS BY MONOCLONAL ANTIBODIES (MEETING ABSTRACT)

Newell KD, Goldenberg DM, Primus FJ
University of Kentucky Medical Center, Lexington, KY, 40536
Fed Proc; 41(3):411 1982

Murine monoclonal antibodies against carcinoembryonic antigen (CEA) were analyzed by radioimmunoassay for immunoreactivity against CEA and the CEA-related antigens, meconium antigen (MA) and nonspecific cross-reacting antigen (NCA). Hybridomas were produced by fusion of P3-X63-Ag8.653 myeloma cells with splenocytes from BALB/c mice immunized with CEA purified from liver metastases of colonic adenocarcinomas. Antibody-antigen binding profiles revealed three classes of hybridomas. Of 87 reactive clones, 8%, 62%, and 30% demonstrated reactivity against CEA, MA, and NCA (class 1), CEA and MA (class 2), and CEA only (class 3), respectively. One hybridoma clone from classes 1 and 3, and two from class 2 were selected for further study. The class 1 and 2 monoclonal antibodies bound similar amounts of the appropriate labeled antigens as that of goat polyvalent CEA or specific NCA antisera. The class 3 monoclonal antibody bound only 50% of the CEA molecules reactive with goat CEA antiserum. Studies using labeled monoclonal antibodies for CEA epitope blocking revealed that the two class 2 monoclonal antibodies lacked the ability to block each other. Thus, these monoclonal antibodies define at least four separate determinants of CEA.

One is shared by CEA, MA, and NCA, two others are shared by CEA with MA, and a fourth appears specific for a subpopulation of CEA molecules. (no Refs)

6. DETECTION AND CHARACTERIZATION OF A MONOCLONAL ANTIBODY-DEFINED MELANOMA ASSOCIATED ANTIGEN WITHIN CIRCULATING IMMUNE COMPLEXES IN NORMAL DONOR SERA (MEETING ABSTRACT).

Morgan AC, Reisfeld RA
Biological Response Modifiers Program, National Cancer Institute-Frederick Cancer Research Foundation, Frederick, MD, 21701
Fed Proc; 41(3):410 1982

We have previously characterized, immunochemically, a glycoprotein of 94,000 MW shed from human melanoma, carcinoma, and fetal uveal melanocytes but not a variety of normal tissues and cells. In the present studies, we found reactivity of monoclonal antibody to this antigen in normal human sera but absent from a variety of animal sera. Gel filtration analysis indicated a heterogenous distribution of reactivity from 2 x 10(5) to 2 x 10(6) MW. Adsorption on Protein-A Sepharose did not remove the reactivity but precipitation with an increasing percentage of polyethylene glycol (PEG) indicated bisphasic removal of antigen. Further analysis, utilizing a reverse sandwich Elisa assay, demonstrated conclusively that antigen reactivity was associated with both IgG and IgM. IgM, associated with antigen, was removed by low concentration of PEG (3.5 percent) whereas IgG, associated with antigen, was not completely precipitated at concentrations as high as 7 percent. These results demonstrate that a human melanoma associated, oncofetal antigen, defined by a xenomonoclonal antibody, is present and elicits a humoral response in normal donors. These results may have important implications for anti-tumor antibody regulation and blockade of host immune responses. (no Refs)

7. MELANOMA-SPECIFIC ONCOFETAL ANTIGEN DEFINED BY A MOUSE MONOCLONAL ANTIBODY (MEETING ABSTRACT).

Liao SK, Clarke BJ, Khosravi M, Dent PB
McMaster University and Ontario Cancer Foundation Hamilton Clinic, Hamilton, Ontario L8N 3Z5, Canada
Proc Am Assoc Cancer Res; 23:1067 1982

Fusion of mouse myeloma cells (P3-NSI-Ag4) with splenocytes from a BALB/c mouse immunized with cultured human melanoma cells (CaCL 78-1) resulted in a hybridoma 140.240, secreting an IgG2a monoclonal antibody which identified an antigen common to all melanomas tested. By direct testing the antibody reacted with 20/20 melanoma lines, but did not react with any of 3 neuroblastoma lines, 5 glioblastoma lines, 13 carcinoma lines, 3 sarcoma lines, 1 teratoma line, 9 fibroblast lines, 1 amniotic epithelial line or 3 xenogeneic tumor lines tested. Quantitative absorption experiments with various cultured and fresh tumors including 7 retinoblastoma cell lines and 5 B-cell lines confirmed the results of direct testing. Furthermore, freshly prepared nevus cells were also non-reactive with this antibody. However, it did react with an antigen on tissue homogenates prepared from fetuses of 10-14 wk gestation. The antigen involved was shed by cultured melanoma lines. Immunoprecipitation and sodium dodecyl sulfate-polyacrylamide gel electrophoresis analysis with lysates of 35S-methionine labelled cell lines indicated that 140.240 identified a single band of 130kd molecular weight only with melanoma lines. Thus the structure identified by monoclonal antibody 140.240 is a melanoma-specific oncofetal antigen. Further characterization of the identified antigen will determine its utility for immunodiagnostic and/or immunotherapeutic purposes. (no Refs)

8. RADIOLABELING OF MONOCLONAL ANTITUMOR ANTIBODIES: COMPARISON OF I-125 AND IN-111-ANTI-CEA WITH GA-67 IN A NUDE MOUSE-HUMAN COLON TUMOR MODEL (MEETING ABSTRACT).

Royston I, Halpern SE, Dillman RO, Stern PL, Hagan PL, Chen A, David GS, Desmond WJ, Adams TH, Bartholomew RM, Frincke JM, Brautigam CE
University of California, San Diego, CA, 92161
Proc Am Assoc Cancer Res; 23:953 1982

Monoclonal antitumor antibodies (MoAbs) labeled with I-131 concentrate in murine tumors. Work in our own laboratory indicates that I-125-anti-CEA (carcinoembryonic antigen) MoABs, while stable in vitro,is dehalogenated in vivo. The following study compared I-125 and In-111-anti-CEA MoAbs with Ga-67 in a nude mouse-human colon tumor model. Anti-CEA was labeled with I-125 using the Bolton-Hunter method, shown to be stable in saline at 37 C over a 72-hr period and to react with specific antigen to 70-80% efficiency. The antibody was conjugated with DTPA (diethylenetriamine pentaacetic acid) using DTPA anhydride, then labeled with In-111. The In-111-anti-CEA complex was stable in vitro with greater than 70% binding to CEA. Nude mice bearing human colon tumors were injected with similar quantities of both isotopes (and 10 uCi of Ga-67) and sacrificed at 4, 24, 48 and 72 hr. Distribution and excretion studies were performed. Tissue concentrations were computed as % injected dose/gm (%ID/G). Peak tumor %ID/G occurred for I-125 (5%) and 4 hr for In-111 (23%) at 62 hr, and for Ga-67 (5%) at 24 hr. Greater than 70% of the I-125 was excreted in the urine by 48 hr, compared to less than 10% of the In-111. Tumor/blood and muscle ratios for In-111-anti-CEA were 8:1 and 39:1 at 72 hr. In-111-anti-CEA MoAbs are superior to iodinated anti-CEA MoAb or GA-67 as a potential tumor imaging agent and should be used preferentially if imaging studies are undertaken with radiolabeled MoAbs in humans. (no Refs)

9. EVIDENCE FOR TUMOR ASSOCIATED FETAL ANTIGEN BINDING TO HUMAN NATURAL KILLER CELLS (MEETING ABSTRACT).

Hogan KT, Harris DT, Evans DL
Bowman Gray School of Medicine, Winston-Salem, NC, 27012
Fed Proc; 41(3):818 1982

TAFA-II, a tumor associated fetal antigen, isolated from methylcholanthrene fibrosarcomas in NBR rats, is biochemically similar to interleukin-1 (IL-1). These peptides have similar molecular weights, pI and amino acid composition. Both modulate cytotoxic T cell activity and induce granulocytosis in the rat. TAFA-II however, has been shown to suppress NK cell activity in humans, rats and mice. The possibility exists that TAFA-II may be an altered form of IL-1, or a member of a related family of peptides which are expressed by tumor cells. We have determined the optimal conditions for TAFA-II binding by human peripheral blood leukocytes (PBL). Binding is greatest at pH 9-11 (4C). Binding is rapid and equilibrium is achieved within 10 minutes. Some individuals demonstrate saturable binding at approximately 10(-13) moles/10(6) PBL. 125I or fluorescein (FITC) labeled TAFA-II was used to identify the cell population which binds TAFA. PBL were pulse labeled with 125I-TAFA-II or FITC-TAFA-II and separated on 40-55% discontinuous Percoll density gradients. Fractions producing the greatest enrichment for NK cell cytotoxicity (K562 targets) had large granular lymphocyte morphology. These same fractions also contained cells (NK and lymphocytes) which bound labeled TAFA-II. These data indicate that

TAFA-II binds NK cells, and as such represents a possible mechanism of regulation of immunosurveillance. (no Refs)

ASSAY PROCEDURES/ SYNTHESIS

10. ON THE LEVEL OF CARCINOEMBRYONIC ANTIGEN IN NORMAL TISSUES AND BIOLOGICAL FLUIDS.

Bobrov IuF, Gamaiunova VB, Stefanenko IuF
N. N. Petrov Res. Inst. Oncology, USSR Ministry Health, Leningrad, USSR
Vopr Onkol; 28(4):34-37 1982

A radio-immunological assay established a high level of carcinoembryonic antigen (CEA) in the saliva of nine patients with colonic tumors and two healthy controls. The antigen was also detected in gastric juice and specimens of mucosa obtained by fibrogastroscopy for 20 cases of gastric pathology. No correlation between CEA levels in saliva and gastric juice was observed. (Author abstract) (3 Refs) (In RUS)

11. BLOOD PLASMA LEVELS OF HORMONES AND CARCINOEMBRYONIC ANTIGEN IN TUMOR AND NON-TUMOR DISEASES OF THYROID.

Ivanov PK, Tkacheva GA
Center Oncology Res., USSR Acad. Medical Sciences, Moscow, USSR
Vopr Onkol; 28(4):29-34 1982

Radioimmunological tests for carcinoembryonic antigen, antibodies to thyroglobulin, thyrotropin of pituitary, thyroxin and triiodothyronine were run in healthy subjects and patients suffering from cervical thyroid and extrathyroid neoplasms, eg nodular goiter, adenoma, cancer, chronic thyroiditis, lymphadenitis, neurinoma, hemangioma and thyrotoxicosis. The thyroid was scanned with 131I or 99mTcO4 in all cases. Scanning of thyroid is the first stage of screening for malignant tumors because 'warm' or 'hot' foci in scanograms of cases of malignant nodes are very rare. In patients with 'cold' thyroid nodes, detection of thyroglobulin antibodies points to thyroiditis since such antibodies are not found in all other cases. None of the indices showed any differences in cases of nodular goiter and 'cold' adenoma. Coefficient sTTH/bTTH (ratio of thyroliberine-stimulated level of pituitary thyrotropin to basal one) is decreased, while coefficient BTTH/T4, BTTH/IFT4 and blood plasma level of carcinoembryonic antigen are increased in patients with thyroid cancer as compared with benign tumors. (Author abstract) (10 Refs) (In RUS)

12. MONOCLONAL ANTIBODIES TO CARCINOEMBRYONIC ANTIGEN (CEA): CHARACTERIZATION AND USE IN A RADIOIMMUNOASSAY FOR CEA.

Lindgren J, Bang B, Hurme M, Makela O
Wistar Inst., 36th St. at Spruce, Philadelphia, PA, 19104
Acta Pathol Microbiol Immunol Scand [C]; 90(3):159-162 1982

Fusion of immune spleen cells of mice immunized with CEA with a mouse myeloma cell line resulted in several hybrid cell lines secreting antibodies to CEA as tested by radio-immunoassay. Four of these were cloned by limiting dilution and large amounts of anti-CEA antibodies were produced by growing the anti-CEA-producing cell clones intraperitoneally in mice and collecting the ascites fluids formed. Ascites fluids containing antibodies with both high and low affinity were obtained. The antibody having the highest affinity was shown to be specific to CEA, whereas one antibody showed crossreaction with the normal cross-reacting antigen (NCA). The establishment of a competitive-inhibition double antibody radio-immunoassay with high sensitivity and specificity using mouse monoclonal antibodies is described. (Author abstract) (15 Refs)

13. RADIOIMMUNODETECTION IN NON-SEMINOMATOUS GERM CELL TUMORS (NSGCT) (MEETING ABSTRACT).

Lange PH, Vogelzang NJ, Fraley EE, Kennedy BJ, Deland FD, Goldenberg DM

No affiliation given

77th Annual Meeting of the American Urological Association, Inc., may 16-20, 1982, Kansas City, Missouri. American Urological Association 254 pp., 1982.

Radioimmunodetection (RID) for localization of CEA (carcinoembryonic antigen)-producing colonic cancer or for AFP (alpha fetoprotein) or hCG (human chorionic gonadotropin) producing germ-cell or trophoblastic tumors using appropriate radioactive labelled antibody has been attempted clinically with promising results. This report describes our experience with RID using 131 Iodine labelled antibody to AFP or hCG in 8 patients (pts) with NSCGT from the University of Minnesota Hospitals. Seven pts had testicular tumors, 1 had a primary retroperitoneal NSGCT. Four pts had elevated AFP (2) or hCG (2) as the only sign of recurrent disease. RID studies suggested disease at specific locations in 3, but surgical explorations of these locations were negative for recurrent disease. In 2 pts in which masses had been detected by other noninvasive methods, RID for anti-AFP (1) or anti-hCG (1) localized the masses accurately. Anti-hCG scans in 1 pt not only localized a known tumor, but detected 2 unrecognized areas which developed overt disease subsequently. The final pt had been successfully treated for a hCG-secreting NSGCT and his anti-hCG scan after chemotherapy was negative. Thus RID was helpful or confirmatory in 50% of pts but misleading or not helpful in the remainder. (1 Ref)

14. DETECTION OF ANTIBODY TO CARCINOEMBRYONIC ANTIGEN BY THE HEMOLYTIC PLAQUE ASSAY.

Stinson RS, Lockhart CG, Margraf HW, Philpott GW

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Int Arch Allergy Appl Immunol; 68(2):134-137 1982

A modification of the standard hemolytic plaque-forming cell assay is described. The conjugation of a soluble antigen, carcinoembryonic antigen, to the membrane of the sheep red blood cell was accomplished and used as the indicator system to detect antibody-forming cells. The specificity of the assay was determined by cross-reacting studies and competitive inhibition by antigen blocking. (Author abstract) (15 Refs)

EXPERIMENTS IN ANIMAL SYSTEMS

15. THE EXPRESSION OF ALPHA-FETOPROTEIN AND ALBUMIN GENES IN RAT LIVER DURING CHEMICAL CARCINOGENESIS.

Schwartz CE, Gabryelak T, Smith CJ, Taylor JM, Chiu JF

(c/o Chiu) Dept. Biochemistry, Univ. Vermont Coll. Medicine, Burlington, VT, 05405

Biochem Biophys Res Commun; 107(1):239-245 1982

The expression of alpha-fetoprotein (AFP) and albumin genes in neoplastic and preneoplastic livers of Fischer rats treated with the hepatocarcinogen 3'-methyl-4-dimethylaminoazobenzene (MDAB) was investigated. The concentration of AFP started to increase in the serum of rats shortly after the initiation of feeding with MDAB (0.06% of the diet). It reached a peak at about 40 days and then decreased dramatically. After 164 days of treatment, serum levels of AFP increased markedly concomitant with the appearance of palpable liver tumors. The final permanent elevation of AFP was associated with the appearance of malignant cells. There was little if any change in the serum albumin concentrations in rats treated with MDAB. Synthesis of AFP in livers of MDAB-treated rats was found to increase in parallel with AFP serum concentrations. Biosynthesis of albumin showed no changes during hepatocarcinogenesis. These results indicate alteration in the control of gene expression during neoplastic transformation. (29 Refs)

16. A COMPARISON OF CARCINOGEN INDUCED OVAL CELL PROLIFERATION AND CHEMICALLY INDUCED BILE DUCT PROLIFERATION IN RAT LIVER (MEETING ABSTRACT).

Sell S

University of California, San Diego, La Jolla, CA, 92093

Fed Proc; 41(3):378 1982

' Oval' cells which appear in the livers of rats exposed to chemical hepatocarcinogens are believed to be of bile duct origin. In order to study this, alphafetoprotein (AFP) production and morphologic changes in the livers of rats fed 0.05% N-2-fluorenylacetamide in a choline devoid diet (CD-FAA) were compared to those induced by feeding 0.15% 4,4'diaminodiphenylmethane (DDPM). Following a two-week feeding of CD-FAA, proliferation of 'oval' cells begins in the portal area and extends rapidly across the liver lobule. Bile duct-like structures are found throughout the liver lobule as a late component of oval cell proliferation. Associated with these changes is a rapid and high elevation of serum AFP and many of the oval cells and duct-like structures contain AFP and albumin when examined by immunofluorescence. Normal bile ducts do not contain AFP or albumin. In contrast, DDPM produces a progressive proliferation of bile ducts, extending from the portal area into the adjacent liver lobule. This is not associated with AFP elevation in the serum and the newly formed ducts do not contain AFP or albumin. It is concluded that the duct-like structures seen as a component of oval cell proliferation do not necessarily represent differentiation of oval cells into bile ducts. Oval cells may have a stem-like capacity to form cell types not seen in the normal adult or fetal liver. (no Refs)

17. EFFECTS OF HEXAMETHYLENE BISACETAMIDE (HMBA), SODIUM BUTYRATE (BA) AND DIMETHYL SULFOXIDE (DMSO) ON ALPHA-FETOPROTEIN (AFP), ALBUMIN AND TRANSFERRIN PRODUCTION BY A HEPATOMA CELL LINE IN SERUM-FREE MEDIUM (MEETING ABSTRACT).

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National Cancer Institute, Bethesda, MD, 20205

Proc Am Assoc Cancer Res; 23:145 1982

Low molecular weight compounds such as DMSO and BA are known to modulate the production of AFP, albumin and transferrin in hepatoma cell lines. In order to further study these effects of DMSO, BA as well as HMBA, growth of rat hepatoma cell line McA-RH 7777 (7777) was obtained on plates precoated with human fibronectin in a serum-free medium. Concentrations of AFP, albumin and transferrin were determined by radioimmunoassay. The medium consisted of 1:1 mixures of Ham's F-12 and Dulbecco's modified Eagles supplemented with insulin, iron saturated transferrin and selenium and 15 mM Hepes. The production of AFP, and transferrin was 200-350 and 15-30 ng/ 10(5) cells/24 hr, respectively. Albumin was nondetectable. Treatment with BA induced a dose-dependent increase in synthesis of AFP and transferrin whereas treatment with HMBA and DMSO caused a dose-dependent decrease in the synthesis of both AFP and transferrin. No induction of albumin synthesis was observed. Similar effects of all three agents on 7777 are observed after treatment with DMSO and BA in serum supplemented medium, except that albumin synthesis was induced 6-fold with BA and HMBA induced AFP synthesis 2-fold. The capacity of BA (4 mM) to induce albumin secretion and of HMBA (4 mM) to induce AFP secretion under serum containing growth conditions but not in defined medium may reflect an absence of permissive factor(s) in the defined medium. (1 Ref)

18. THE ROLE OF VIRAL AND ONCOFETAL ANTIGENS IN MURINE LYMPHOSARCOMA METASTASIS TO SPECIFIC SITES (MEETING ABSTRACT).

Nicolson GL, Reading CL, Mascali JJ, McGuire EJ

Department of Tumor Biology, The University of Texas Cancer Center System, M. D. Anderson Hospital and , Tumor Institute Houston, TX, 77030

Proc Am Assoc Cancer Res; 23:181 1982

Metastatic variants of murine RAW117 lymphosarcoma were established by sequential selection in vivo for enhanced liver or lung colonization or in vitro for decreased binding to the immobilized-lectins Con A, WGA, RCA (concanavalin A, wheat germ agglutinin, red cell agglutinin) and PNA. The heterogeneity and stability of the selected sublines were examined using cloning techniques. Cell surface analysis of sublines and clones indicated that loss of cell surface viral envelope glycoprotein gp70 correlated well with metastatic properties suggesting that host response may be involved. A variety of in vivo experiments indicated that host macrophages may suppress high gp70 containing clones but allow growth of low gp70 containing clones. To determine the role of cell surface oncofetal antigens in organ colonization we tested the effects of antibodies made against fetal liver cell adhesion components. Liver specific colonization was blocked by pretreatment with Fab' or F(ab')2 antibodies made against the embryonic liver cells. The liver colonizing RAW117 sublines appear to have higher levels of the oncofetal antigen(s) compared to parental or lung colonizing tumor cells. (2 Refs)

IMMUNOLOGIC INTERACTIONS

19. IMMUNOLOGICAL SIMILARITY OF CEA AND ALPHA1-ACID GLYCOPROTEIN (OROSOMUCOID).

Ochi Y, Fujiyama Y, Hosoda S, Miyazaki T, Yoshimura M, Hachiya T, Kajita Y
Second Dept. Internal Medicine, Shiga Univ. Medical Science, Seta, Otsu, Shiga, 520-21, Japan
Clin Chim Acta; 122(2):145-160 1982

Carcinoembryonic acid (CEA) labeled with 125I could be precipitated by antibody to alpha1-acid glycoprotein (AG) in a dose-dependent manner. CEA preparations showed cross reactivity with three kinds of commercial anti-AG preparations by polyethylene glycol and by a double antibody method. The radioactive peak of 125I-CEA showed cross-reactivity with commercial anti-AG and with antisera to purified AG preparations. The binding of 125I-CEA with anti-AG was displaceable by purified AG. Thus, CEA and AG are immunologically similar, although antibody against CEA showed no cross-reactivity with AG. The CEA molecule may have a component that is immunologically similar to AG and it may be in the protein part. CEA purified from hepatic metastases of a primary adenocarcinoma of the colon was subjected to anti-AG sepharose affinity chromatography, eluted and labeled with 125I. Fractionation revealed a peak with extremely high immuno-reactivity with both anti-AG and anti-CEA and a large molecular protein with both AG and CEA antigenic determinants. Studies of the immunoreactivity of this large mol wt fraction demonstrated that the immunoreaction of CEA with anti-AG was a non-precipitation reaction. Based on differences in binding affinities between CEA with anti-CEA and with anti-AG, it was postulated that CEA may be a biosynthetic precursor of AG or pro-AG. (38 Refs)

20. IMMUNE REACTANTS CHANGES AND THEIR RELATIONSHIP TO TUMOR BURDEN IN MALIGNANT MELANOMA (MM) (MEETING ABSTRACT).

Salinas FA, Wee KH, Silver HK
Cancer Control Agency of British Columbia, Vancouver, British Columbia, Canada
Proc Am Soc Clin Oncol; 1:C-137 1982

We have reported the interaction of antibody (Ab) and oncofetal antigen (Ag) in MM patients' (pts) sera, and have shown how their absolute and relative levels regulate the concentration, size and composition of associated immune complexes (IC). Sucrose gradient fractionation (SGF) demonstrated that group (Gp) II pts' sera having Ab and Ag ratios close to equivalence contained predominantly large (greater than 16S) while Gp I and III pts' sera having Ab and Ag excess showed small (7-9 S) and medium (10-15 S) IC respectively. Now we performed further analysis of the immune reactants involved. Melanoma associated antigen (MAA) isolated by Raji-cell bound IC method from pts' sera upon isolectric focusing showed a single pI 4.3 band. When optimally reacted (3 ug) with both autologous and allogeneic MM pts' sera (50 ul of 1:8 diluted) combinations resulted in a sequence of breakdown or formation of IC respectively. While the former is observed in Ag excess (Gp III pts), the latter occurred in Ab excess (Gp I pts). Upon autologous combinations a series of IC size growth followed by breakdown to de novo formation of limiting size moieties (7.7 S) was observed. Allogeneic combinations resulted in IC size increase for Gp I, unchange for Gp II, and decrease for Gp III pts' sera. (no Refs)

CLINICAL/ DIAGNOSIS/ IMMUNOTHERAPY

21. THE PROGNOSTIC VALUE OF CEA DETERMINATIONS IN THE PLASMA OF PATIENTS WITH SQUAMOUS CELL CANCER OF THE CERVIX.

Kjorstad KE, Orjasaester H
Norwegian Radium Hosp., Montebello, Oslo 3, Norway
Cancer; 50(2):283-287 1982

One hundred and ninety-five patients with squamous cell cancer of the cervix have been followed for 2-4 yr. Pretreatment CEA determination was of prognostic value only in patients with early clinical disease. Serial determinations of CEA after primary treatment are of limited value in advanced stages. Sixty-five percent of patients developing recurrent cancer after initial therapy for Stage IB disease had plasma CEA levels exceeding 5.0 ug/l. In many of these cases the CEA elevation preceded the clinical diagnosis by several months. (Author abstract) (15 Refs)

22. ANDROGEN STIMULATION OF BREAST CYST FLUID ANTIGEN LEVELS IN PLASMA OF PATIENTS WITH METASTATIC BREAST CARCINOMA (MEETING ABSTRACT).

Dilley WG, Leight GS, Wells SA
Duke University Medical Center, Durham, NC, 27710
Proc Am Assoc Cancer Res; 23:603 1982

In reviewing patients receiving androgen therapy for metastatic breast carcinoma, it was noted that plasma levels of gross cystic disease fluid protein (GCDFP-15) frequently became markedly elevated in a short time. To confirm this finding, 9 patients (age 57-75 yr) were admitted to the Duke Clinical Research Unit and administered fluoxymesterone (10 mg tid) for 6 days. During the first 4 days plasma GCDFP-15 and carcinoembryonic antigen (CEA) levels were obtained 4 times daily and during the last 2 days they were obtained twice daily. Twenty-four hour urines were collected daily. Blood was analyzed for GCDFP-15 by a previously described RIA (radioimmunoassay) and for CEA by the Roche CEA RIA kit. Urines were analyzed for GCDFP-15. Six patients increased their plasma GCDFP-15 levels markedly (range 102-800%) by the sixth day of therapy; two had lesser increases (20% and 82%) and one had a decrease. Five patients had increases in plasma CEA (7 to 81%) and 4 patients had decreases (-2 to-22%). The differences between the changes in CEA and GCDFP-15 were significantly different. Urinary 24 hour output of GCDFP-15 was increased by at least 100% in 6 of the patients (range 101-1646%). These observations may provide the basis for a provocative test for detection of disease recurrence in patients with breast carcinoma. (no Refs)

23. TUMOR MARKER EXPRESSION IN INTERVAL BREAST CARCINOMAS (MEETING ABSTRACT).

Halter SA, Dupont WD, Hartmann WH
Departments of Pathology and Preventive Medicine, Vanderbilt Medical School, Nashville, TN
Lab Invest; 46(1):33A 1982

American Cancer Society-National Institutes of Health Breast Cancer Detection and Demonstration Projects (BCDDP) screened women annually for breast cancer. Women with negative mammograms at initial screen who presented before the next screen with histologically proven breast cancer were labeled interval cases. Twenty-three interval cases observed at the Vanderbilt BCDDP were compared with 31 age-, parity-, and family history-matched controls whose cancers were detected at annual screen. The expressions of carcinoembryonic antigen (CEA) and the gp 52 antigen related to the mouse mammary tumor virus were studied using immunoperoxidase techniques. The average age of all patients was 52 years. Seventeen per cent of interval patients were nulliparous and 30 per cent had a family history of breast cancer. Seventy-eight per cent of interval cases had infiltrating ductal carcinomas compared with 54 per cent of controls. Tumor size averaged 1.9 cm in both groups. No significant difference was found in presence of fibrocystic disease or breast side involved. Interval cases had an average of seven positive lymph nodes compared with two in controls. The presence of calcium in the tumors was significantly different between the two groups. Carcinoma in situ was present in significantly more control tissues. Blocks were available from 17 interval breast cancer cases and 26 matched controls. Sixty-five per cent of interval cases expressed CEA compared with 57 per cent of controls. Only two interval cases expressed gp 52 compared with 11 controls. (no Refs)

24. THE CLINICAL IMPORTANCE OF PLACENTAL ALKALINE PHOSPHATASE AS A TUMOR MARKER IN SEMINOMA (MEETING ABSTRACT).

Lange PH, Vessella RL, Millan JL, Stigbrand T, Ruoslahti E, Fishman WH
No affiliation given
77th Annual Meeting of the American Urological Association, Inc., may 16-20, 1982, Kansas City, Missouri. American Urological Association 254 pp., 1982.

It is well established that serial determinations of the serum tumor markers alpha-fetoprotein (AFP) and human chorionic gonadotropin (hCG) are often indispensable in the management of nonseminomatous germ cell tumors (NSGCT). However, serum tumor markers are much less established for patients with pure seminoma (Sem): AFP is never elevated and hCG only in about 10-20%. Placental alkaline phosphatase (PlAP) is an oncodevelopmental enzyme normally produced by trophoblastic tissue. It was occasionally found in Sem but insensitive catalytic assays precluded assessment of its clinical value. We studied the prevalence and clinical usefulness of serum PlAP using a sensitive enzyme-linked immuno-assay (ELISA) whose upper limit of normal is 1.85 ng/ml. Seventy-seven patients (200 sera) were studied: 28 with active Sem, 22 with active NSGCT, and 36 controls including 30 with inactive testicular tumor. Serum PlAP levels were elevated in 16/28 with active Sem. Ten of the 16 also had elevated hCG and 71% overall had elevated hCG and/or PlAP. No PlAP elevations were present among controls. In serial studies of 13 Sem patients, PlAP levels were often discordant with hCG or were the only markers elevated, and provided unique clinical information in 6. In active NSGCT, PlAP levels were elevated in only 2/22 and did not provide important clinical information in serial studies. Both serum PlAP and hCG levels should be monitored in Sem patients using sensitive immunological assays. (no Refs)

25. EMBOLIZATION IN HEPATIC TUMOURS.

Nunnerley HB
Dept. Diagnostic Radiology, King's Coll. Hosp., Denmark Hill, London SE5 9RS, England
Excerpta Med Int Congr Ser; 575:66-71 1982

Embolization of hepatic benign and malignant tumors is discussed. Metastases are the commonest tumor found in the liver. If pain is particularly dominant because of the extent of the tumor or if the tumor is endocrine secreting (carcinoid) embolization is advisable. Patients with carcinoid metastases require a particular care and a pre-operative control of the hormone secretion. Any abnormality in clotting factors must be observed and the procedure has to be covered with antibiotics; penicillins and metronidazole should be administered for at least 10 days. Twenty-six patients (20 males, 6 females, 16-68 yr old) with malignant hepatomas were treated. Nine of the patients were Australian antigen positive, 13 had raised alpha-fetoprotein (AFP). After embolization a significant decrease in AFP levels was observed. Indications for a successful outcome from embolization are localized tumor, non cirrhotic liver, jaundice caused by compression of major ducts, pain, and association of the tumor with hormonal manifestations. Contraindications are cirrhosis, diffuse extensive tumor, obviously previous arterial ligation, and portal vein occlusion. Majority of patients with primary tumors are treated with chemotherapy, with or without embolization. Patients with benign tumors can be treated with embolization alone. (3 Refs)

26. AN IMMUNOHISTOCHEMICAL 5'-NUCLEOTIDE PHOSPHODIESTERASE METHOD FOR THE DIAGNOSIS OF LIVER CANCER IN HUMAN LIVER BIOPSY (MEETING ABSTRACT).

Tsou KC, Lo KW, Witzleben CL, Suganuma T
Department of Surgical Research, University of Pennsylvania, Philadelphia, PA, 19104
Proc Am Assoc Cancer Res; 23:67 1982

Serum 5'-nucleotide phosphodiesterase isozyme (5'-NPD-V) has been reported as a useful test for liver cancer. In the course of the study of the development of the isozyme, a pure human 5'-nucleotide phosphodiesterase has been isolated from normal liver specimen with diethylaminoethanol (DEAE)-Sephacel or concanavalin A (ConA)-Sepharose 5B chromatography. Anti-sera of this enzyme was prepared from rabbits and tested in an immunohistochemical procedure, using peroxidase-antiperoxidase (PAP) method, and diaminobenzidine (brown), as a substrate. To avoid hemosiderin in liver, a new method developed by us using 4-dimethylamino-1-naphthylamine and 2,5-dihydroxy-naphthalene (blue) were also used. The tumor cells in liver stain 2 to 3 times darker than the surrounding normal liver in all six cases hepatocellular carcinoma examined and one case of metastasized liver. Carcinoembryonic antigen stains also weakly and alpha fetoprotein faintly or none in the same tumor area. In cirrhotic area this enzyme is present but not elevated. Orcein stain for HBsAg (Shikata) also found positive in tumor area 2/3 patients whose sera was HBsAg negative, and negative in 2/2 patients whose sera was HBsAg positive. These findings further support the suggestion that 5'-NPD is a growth related enzyme. This study supports the oncofetal expression of the 5'-NPD in tumor and the heterogeneity of antigen expression in liver cancer. (no Refs)

27. AGGRESSIVE THERAPY OF LIVER METASTASES (MEETING ABSTRACT).

Laufman LR, Guy JT, Nims TA, Guy JF, Courter SG
Grant Hospital, Columbus, OH, 43215
Proc Am Soc Clin Oncol; 1:C-374 1982

Seventeen patients with unresectable liver metastases from colon cancer were treated with hepatic artery ligation and infusion chemotherapy via a Raimondi catheter sutured into the portal vein. Three patients, all of whom had extensive extrahepatic disease, expired postoperatively. The fourteen evaluable patients received at least one course of Mitomycin C 10 mg/M2 bolus, day 1 and 5-Fluorouracil 1200 mg/M(2)/24 hours days 1-5. Both were administered through the portal vein catheter and were repeated q 56 days and q 28 days respectively. Toxicity consisted of thrombocytopenia due to Mitomycin C, and occurred in six patients (42%). Patient acceptance was superb because most courses were administered as outpatients using a Cormed infusion pump. All patients had a dramatic decrease in CEA (carcinoembryonic antigen), except two who were normal initially. Complete remissions, documented at surgical exploration, occurred in two patients, who remain alive at 20+ and 38+ months. For the fourteen evaluable patients, average survival from date of surgery is 13.3+ months, with three patients alive at 16+, 20+, and 38+ months. We believe that this aggressive approach is indicated in patients who have unresectable liver metastases as their sole manifestation of colon cancer, or in carefully selected patients with liver metastases as their major symptomatic site. (no Refs)

28. COMBINATION CHEMOTHERAPY WITH DOXORUBICIN AND STREPTOZOTOCIN (DXR/STZ) IN HEPATOCELLULAR CARCINOMA (HC) (MEETING ABSTRACT).

Morstyn G, Ihde DC, Eddy JL, Bunn PA, Cohen MH, Minna JD
National Cancer Institute-Navy Medical Oncology Branch, National Naval Medical Center, Bethesda, MD, 20814
Proc Am Assoc Cancer Res; 23:523 1982

Twenty-three patients with unresectable HC were given DXR 60 mg/m2 IV Day 1 and STZ 0.5 g/m2 IV Days 1-5 every 3 weeks. This regimen was chosen because of the activity of DXR and nitrosoureas in HC and the ability to administer both drugs in full doses. Twelve patients were fully ambulatory, 14 had normal serum bilirubin, 11 had pathologic proof of cirrhosis, and 11 had no known extrahepatic tumor dissemination. Partial response lasting 10 and 14 months occurred in 2 patients (9%), 1 had stable disease for 12+ months, 12 had documented tumor progression within 4 months, and 8 died within 6 weeks of the start of DXR/STZ. Median survival of all patients was only 3 months, but 8 (35%) lived more than 1 year. Of these 8, 2 responded to DXR/STZ, another 2 to subsequent chemotherapy, and 4 had no tumor response whatever. More than 90% of the intended doses of DXR/STZ was administered, with severe leukopenia in 1 patient, severe thrombocytopenia in 3, and moderate proteinuria in 9. Various physical, radiologic, and bio-chemical parameters were assessed for their utility in detecting tumor response and progression. Initially abnormal physical examination of the liver, hepatic radionuclide and computed tomographic (CT) scans, and serum alpha-fetoprotein (AFP) levels improved in both responding patients. (no Refs)

29. MEDULLARY CANCER OF THE THYROID. CLINICAL FORMS, DIAGNOSTIC AND THERAPEUTIC APPROACHES.

Rougier P, Travagli J, Schlumberger M, Caillou B, Lacour J, Gardet P, Parmentier C
Institut Gustave-Roussy, 39-53, rue Camille-Desmoulins, 94805 Villejuif, France
Rev Prat; 32(29):1997-2003 1982

Medullary thyroid (MTC) is a rare tumor of the thyroid which does not take up Iodine and is not influenced by thyroid stimulating hormone. Initial symptoms may include cervical nodules or functional signs such as diarrhea and flush. Diagnosis and surveillance of MTC is based on thyrocalcitonin and carcinoembryonic antigen. Treatment of choice is surgical excision. In cases where familial form of MTC is prevalent, relatives of patients should be screened for the disease. Post-treatment prognosis is good. (19 Refs) (In FRE)

30. DIAGNOSTIC VALUE OF CARCINOEMBRYONIC ANTIGEN IN PLEURAL FLUID.

Heyenga H, Morr H
Klinik Waldhof Elgershausen, 6349 Greifenstein, W. Germany
Dtsch Med Wochenschr; 107(21):818-821 1982

Of 30 unselected patients with pleural effusion of unknown cause 17 were subsequently found to have malignant disease of the pleura. In 11 of the 17 patients the concentration of carcinoembryonic antigen (CEA) in the pleural effusion was elevated to 4-60 ng/ml. In all 13 patients with pleural effusion of nonmalignant cause the CEA concentration was normal (0-2 ng/ml). While the specificity of CEA antigen was 100% in the diagnosis of malignant pleural disease, its sensitivity was only about 65%. Since low CEA values in pleural effusion thus cannot exclude malignant disease with certainty, histological assessment of the pleural disease should be practiced in every case where tumor is suspected, if necessary via thoracoscopy or thoracotomy. (Author abstract) (11 Refs) (In GER)

31. THE VALUE OF CARCINOEMBRYONIC ANTIGEN AND TENNESSEE ANTIGEN IN DIAGNOSIS OF RECTAL CARCINOMA.

Brockamp G, Braun J, Langer S
Abteilung Chirurgie der Medizinischen Fakultat, RWTH Aachen, Goethestr. 27/29, D-5100 Aachen, W. Germany
Aktuel Chir; 17(3):99-101 1982

Forty-five patients with histologically confirmed adenocarcinoma of the rectum were tested preoperatively for carcinoembryonic antigen (CEA) and Tennessee antigen (TAG) in their sera. Abnormally high CEA levels were found in sera of 22 of the patients and abnormally high TAG levels in sera of 39. The TAG levels were abnormal in 21/23 patients with normal CEA levels, while the CEA levels were abnormal in 2/6 patients with normal TAG levels. No relationship was found between tumor stage and level of CEA or TAG. (30 Refs) (In GER)

32. PROVIDING FOLLOW-UP IN CHILDHOOD CANCER.

Napolitano LV, D'Angio GJ, Grossfeld JL, Mauer AM, Miller DR, Sinks LF, Peterson RD
(c/o Editor) Patient Care, 16 Thorndal Circle, Darien, CT, 06820
Patient Care; 16(13):167-169,173,176-178,180,182,187-188,190-192 1982

Consequences of therapy in childhood cancer patients are discussed. Findings indicate a drop of 10 or more points in IQ score in children who received 2,400 rad to the brain plus systemic methotrexate. Radiation and cyclophosphamide can cause aspermia, oligospermia, amenorrhea, and, less frequently, the absence of secondary sexual maturation. Exostoses may appear after radiation therapy; these represent derangements of growth rather than benign tumors. Children who have had surgery and who have been treated with bleomycin sulfate may exhibit pulmonary problems upon re-operation. The risk of a second cancer is approx 12% 25 yr posttreatment. Various genetic clusters of diseases appear to be associated with a high incidence of secondary malignant neoplasms. Patients with von Recklinghausen's disease have a tendency to develop neurofibrosarcoma. In follow-up, the former patient is checked monthly at first, then every 6 wk, every 3 mo, and annually by the fifth yr posttreatment. More organized cooperative study follow-ups can help to define and answer some of the questions of long-term side effects of therapy. The presence of alpha-fetoprotein and human chorionic gonadotropin on laboratory assays can be considered as possible signs of germ cell tumors and hepatocellular carcinoma. Cancer 'cure' can only be defined by studying data on large numbers of patients and finding the cut-off point in time after which recurrence of the specific cancer has been highly unusual. Second-line treatment should be administered if no remission occurs and in case of relapse. (5 Refs)

33. PALLIATION OF PELVIC RECURRENCE OF COLORECTAL CANCER BY INTRA ARTERIAL CHEMOTHERAPY (MEETING ABSTRACT).

Peters RE, Patt YZ, Chuang VP, Wallace S, Fuqua R, Mavligit GM
M. D. Anderson Hospital, Houston, TX, 77030
Proc Am Soc Clin Oncol; 1:C-147 1982

Pelvic recurrence of colorectal cancer (CRC) is a difficult management problem. Obstruction of urinary and fecal streams may be diverted; however, the severe pain may be refractory. Currently, radiotherapy is the best mode of therapy. We have given palliative intra-arterial chemotherapy to 10 patients. Seven had failed radiotherapy and 4 had also failed intravenous chemotherapy. The technique involved placement of bilateral internal iliac arterial catheters percutaneously. Nine patients were treated with intra-arterial mitomycin C and 5-fluoropyrimidine by continuous infusion, and 1 was additionally treated with adriamycin. Six of 7 patients with increased Carcinoembryonic Antigen (CEA) had a partial response (PR) (greater than 50% reduction in CEA). Two of these patients had rapidly rising creatinine and hydronephrosis at the beginning of therapy. Both had re-establisment of urinary flow and return of creatinine to normal. One of the 7 patients had subjective pain relief with no change in CEA. Of the 3 patients with normal CEA, symptoms improved in one, were unchanged in the second and increased in the third. Overall, pain relief was observed in 80%. The major side effect was a chemical dermatitis over the perineum and gluteal region. The extent ranged from minimal to severe (2 cases). The severity of the cutaneous reaction could possibly be ameliorated by steroids. Mucositis was seen in 2 patients. One patient sustained a mild L-5 neuropathy after catheter displacement. We conclude that iliac artery infusion of 5-FU + mitomycin C could offer palliation to patients with pelvic recurrence of CRC who have failed other treatment modalities. (no Refs)

34. EFFECTIVE CONTROL OF LIVER METASTASES FROM COLON CANCER WITH AN IMPLANTED SYSTEM FOR HEPATIC ARTERIAL CHEMOTHERAPY (MEETING ABSTRACT).

Ensminger W, Thrall J, Cozzi E, Doan K
Departments of Medicine and Surgery, University of Michigan, Ann Arbor, MI, 48109
Proc Am Soc Clin Oncol; 1:C-363 1982

A totally implanted delivery system for hepatic arterial chemotherapy has been evaluated in 60 patients with liver metastases from colorectal cancer. Silastic catheters were surgically implanted to deliver drug to the entire liver and connected to subcutaneously placed pumps. Pumps were refilled every 2 weeks alternating floxuridine (FUDR, 0.3 mg/kg/d) with normal saline. Hepatic tumor response was assessed by liver scan (LS) and physical examination (PE), aided by carcinoembryonic antigen (CEA) measurements. Thirteen thousand days of outpatient infusion and greater than 900 refills have been given without infection, bleeding or arterial thrombosis. Eighty-three percent (50/60) of patients responded, 15% (9/60) had stable disease and 2% (1/60) had progressive disease by LS/PE. Ninety-eight percent (47/48) of patients had a greater than 50% reduction in CEA. No patients with hepatic only disease have died. Sixty-six percent of patients are still alive. Median survival by life table analysis from diagnosis of hepatic metastases exceeds 21 months. Median survival by life table analysis for patients with extrahepatic disease at implant is 7 months and for those developing extrahepatic disease is 10 mo from time of implant. Toxicities have all been reversible and consist of gastritis (60%), ulcers (8%), and anicteric (23%) and icteric (23%) hepatitis. (no Refs)

35. SERUM ANTIGEN TUMOR MARKER FOR COLON CARCINOMA: (MEETING ABSTRACT).

Sears HF, Koprowski H, Herlyn M, DelVillano B, Steplewski Z
The Wistar Institute, Philadelphia, PA, 19104
Hybridoma; 1(2):217 1982

We have shown that a monoclonal anticolorectal cancer (CRC) antibody can identify a tumor associated antigen in the sera of 70% of patients with advanced CRC. We used two monoclonal antibodies which bind to monosialogangliosides on the surface of CRC cells to identify these tumor associated glycolipids in the serum of 85 patients with primary CRC tumors. The results were compared to these patients' stage of disease and their CEA (carcinoembryonic antigen) levels. We studied longitudinally collected sera of these patients at high risk for recurrence. We were able to test all the sera from one patient at one time because of the stability of the antigen. Sixty-six of 85 patients had at least one antigen elevation in the perioperative period, 39 detected by antibody 52A binding inhibition, 42 detected by direct RIA (radioimmunoassay) using antibody 19-9, and 37 by CEA. Levels were not related to Dukes' stage (A-C). The presence of one antigen did not predict the presence or absence of another antigen. Six antigens were not detected preoperatively in patients in whom the antigen was detected in the follow-up period prior to detection of clinical recurrence. The decay of antigen level by 7 days after the removal of the primary tumor was erratic and not predictive of recurrence. Twelve of the 35 patients with B2 or C stage primary tumor have had a recurrence. Sera for serial assays was obtained every 3 months. Antigen elevations in these longitudinally collected sera predicted the recurrences by at least 3 months to as much as 18 months prior to clinical discovery in 10 of the 12 patients. In 7 patients, one of the monoclonal-antibody-identified-antigens never returned to normal, and in 3 patients antigen levels fell only to rise again many months prior to clinical recognition of recurrence. (no Refs)

36. DIAGNOSTIC ROLE OF ALPHA-FETOPROTEIN DETERMINATION IN SERUM OF PATIENTS WITH MALIGNANT TESTICULAR NEOPLASMS.

Akhverdova LN, Nanobashvili DM
Georgian Cancer Res. Center, Tbilisi, USSR
Urol Nefrol (Mosk); (3):23-26 1982

Diagnostic efficacy of determination of serum alpha-fetoprotein (AFP) was studied in 91 patients with testicular neoplasms. Among these patients, 17 had teratoblastomas, 5 had mixed tumors, 1 had embryonal carcinoma, 1 had chorioepithelioma, 60 had seminomas, 1 had fibrosarcoma, 4 had carcinomas, and 2 had adenomas. AFP levels were assayed by a conventional precipitation method and by indirect immunoautoradiography (IR) technique. Precipitation method showed presence of AFP in the serum of 8/17 patients with teratoblastoma and in 2/5 patients with mixed tumors. The use of IR technique in the patients with negative results of precipitation tests showed AFP in nine additional patients (7/9 with teratoblastoma and 2/3 with mixed tumors). The IR test also showed the presence of

FAP in one patient with embryonal carcinoma. Successful treatment resulted in disappearance of AFP. Repeated elevation of AFP was indicative of metastases or recurrence. (14 Refs) (In RUS)

37. RESTAGING IN TESTICULAR CANCER, PROGNOSIS WITHOUT RADICAL DISSECTION (MEETING ABSTRACT).

ten Bokkel Huinink WW, Van Dongen JA, Delemarre JF, McVie JG
Netherlands Cancer Institute, 1066 CX Amsterdam, The Netherlands
Proc Am Soc Clin Oncol; 1:C-466 1982

From 1977 55 pts with stage II and III testicular cancer were treated with cisplatin, vinblastine and bleomycin. In 27 cases there was a discrepancy at the end of 4 courses of chemotherapy consisting of normalization of beta subunit HCG (human chorionic gonadotropin), AFP (alpha fetoprotein) or LDH (lactic dehydrogenase) and persisting abnormalities on x-rays or CT (computer tomography) scans. A restaging procedure was therefore performed: 18 laparatomies and 9 thoracotomies. Residual 'tumor' tissue was biopsied or where appropriate, removed without any attempt to do radical retroperitoneal dissection or aggressive debulking. Resection of all tumor rests was incomplete in 4 of the 8 pts proven to have residual vital tumor at operation; one had diffuse lung metastases and 3 had completely fixed tumor masses. All pts with tumor positive findings continued further chemotherapy, one subsequently entered CR (complete response). Survival of this group of 27 men, 72%, is not worse than of the total cohort of 55 pts: 65%, with a median follow-up of greater than 1 year. Of the surgically 'complete' treated pts with vital tumor 3 of 4 survived (2-10 months), one died of brain metastases. None of the surviving pts is impotent or suffers from retrograd ejaculation. These figures suggest that extended resection is only necessary if vital tumor is found during restaging procedure. One should consider not doing radical resection if frozen section biopsies during surgery reveal mature teratoma or necrotic tissue. (no Refs)

38. EXTRAGONADAL SEMINOMAS (MEETING ABSTRACT).

Caracandas JE, Friedman M, Panahon AM, Wajsman Z, Johnson R
Roswell Park Memorial Institute, Buffalo, NY, 14263
Proc Am Soc Clin Oncol; 1:C-454 1982

Extragonadal seminomas comprise a distinct clinicopathological entity of great interest in view of their potential for cure. From 1966 to 1981 6 of 210 patients with the diagnosis of germ cell tumors were classified as Extragonadal Seminomas. Five had initially mediastinal presentation and 1 retroperitoneal. Two of 6 patients had limited disease and 4 locally extensive disease. Four patients had local irradiation (TD 3000 rads/3wks), one had surgical debulking followed by radiation and the last one chemotherapy followed by radiation. In 5/6 patients AFP (alpha fetoprotein) and HCG (human chorionic gonadotropin) markers were negative. All six had normal testes. Subsequently 4/6 developed disseminated disease and the remaining 2 are alive and free of disease following the initial treatment. One patient was re-classified on subsequent biopsies as Malignant Melanoma. In view of the unpredictable progression of disease in extragonadal seminomas, multimodality management should be the treatment of choice and integration of surgery, radiation and chemotherapy should be employed. (no Refs)

39. YOLK SAC TUMORS (YST) IN CHILDHOOD: PRIMARY TREATMENT WITH CHEMOTHERAPY (MEETING ABSTRACT).

Sartain P, Ducore JM, Buchanan GR
University of Texas Health Science Center, Dallas, TX, 75235
Proc Am Soc Clin Oncol; 1:C-404 1982

YST, or endodermal sinus tumor, is a rare neoplasm of germ cell origin. Prognosis is generally regarded as poor with only 20-50% survival. Since there is little information regarding management we have reviewed treatment in 11 patients with YST seen at our center since 1976. Primary tumors arose in the sacrococcygeal area (4), testicle (3), abdomen (2), ovary (1), and vagina (1). There were five females and six males ranging in age from seven months to three and a half years. Only three patients (all with testicular primaries) had complete surgical resection of the tumor; one patient received post-operative radiation therapy. All 11 were treated with chemotherapy. Primary treatment consisted of vincristine, actinomycin-D and cyclophosphamide (VAC) for 6-24 months in nine patients. In addition, six children with large, unresectable, regional and/or locally recurrent tumors subsequently received vinblastine, bleomycin and cis-diamminedichloroplatinum-II (VBP) for 4-8 months. Serum alpha-fetoprotein determinations, performed serially, were a sensitive indicator of tumor response as well as recurrence. In the two patients with recurrent disease there was rapid tumor lysis after VBP. There was one death due to sepsis; however, the other ten patients are alive and well up to eight years after diagnosis (91% DFS). Our current management includes VAC for six months followed by VBP for four months. (no Refs)

ULTRASTRUCTURE/ CYTOCHEMISTRY

40. GROWTH OF HUMAN HEPATOMA CELL LINES WITH DIFFERENTIATED FUNCTIONS IN CHEMICALLY DEFINED MEDIUM.

Nakabayashi H, Taketa K, Miyano K, Yamane T, Sato J
(c/o Sato) Div. Pathology, Cancer Inst., Okayama Univ. Sch. Medicine, 2-5-1 Shikata-cho, Okayama 700, Japan
Cancer Res; 42(9):3858-3863 1987

A human hepatoma cell line, HuH-7, which was established from a hepatocellular carcinoma, was found to replicate continuously in a chemically defined medium when the medium was supplemented with Na2SeO3. The cells grew better in this medium than in serum-containing medium without any adaptation period. Other established human hepatoma and hepatoblastoma cell lines, HuH-6 cl-5, PLC/PRF/5, huH-1, and huH-4, also grew in the defined medium. Although HLEC-1 cells failed to proliferate continuously with Na2SeO3 alone, they grew if a cell-free conditioned medium from HuH-7 cells was added to the medium. These cell lines, except the HLEC-1 cell line, produced the following human plasma proteins among those examined: albumin, prealbumin, alpha1-antitrypsin, ceruloplasmin, fibrinogen, fibronectin, heptoglobin, hemopexin, beta-lipoprotein, alpha2-macroglobulin, beta2-microglobulin, transferrin, Complement Components 3 and 4, and alpha1-fetoprotein. Beside plasma proteins, the media from HuH-7, HuH-6 cl-5, PLC/PRF/5, and huH-1 contained anti-carcinoembryonic antigen-reactive proteins, and those from PLC/PRF/5, huH-1, and huH-4 medium contained hepatitis B surface antigen. These proteins were detected during periods of serial cultivation over 9 mo under the above culture conditions. The hepatoma cell lines grown in the fully defined synthetic medium may provide a new approach for investigating the growth and metabolism of human hepatoma cells in vitro. (Author abstract) (35 Refs)

41. SEX STEROID HORMONES LEVELS AND TESTICULAR ACTIVITY DURING HEPATOCARCINOGENESIS BY N-2-FLUORENYLACETAMIDE.

Lafaurie M, Aussel C, Castelli D, Krebs B, Stora C
INSERM U 210 (Laboratoire d'Histologie et d'Immunologie), 06034 Nice, France
Res Commun Chem Pathol Pharmacol; 37(1):49-63 1982

During hepatocarcinogenesis by N-2-fluorenylacetamide, the hormonal status of male Sprague Dawley rats is modified. The testes present a reduced activity which is evidenced by a decreased spermatogenetic activity accompanied by a drastic decrease of the plasma testosterone level. In contrast, plasma progesterone and estradiol-17beta levels were not modified despite the 80 fold augmentation of alpha-fetoprotein, an estrogen binding protein synthesized during liver carcinogenesis. (Author abstract) (27 Refs)

42. THE LIMITS TO THE RELIABILITY OF BIOLOGICAL TUMOR MARKERS IN NONSEMINOMATOUS TESTIS TUMORS.

Boccon-Gibod L, Elias D
Clinque Urologique, Hopital Cochin, 27, rue du Faubourg Saint-Jacques, 75674 Paris, France
Ann Urol (Paris); 16(4):219-220 1982

Before castration the levels of alphafetoprotein and chorionic beta-gonadotropin were normal in six patients, three of whom had retroperitoneal metastases (RM). In nine patients (4 of whom were free of RM), levels of the markers were elevated. After castration, 3/10 patients with normal marker levels had RM. In five cases in which levels were elevated, all patients had metastases. No RM developed in patients whose levels normalized following castration. (10 Refs) (In FRE)

REVIEWS/ OTHER RELATED STUDIES

43. FETAL AND ONCOFETAL ANTIGENS. REGULATORS OF IMMUNE REACTIONS.

McCluskey DR
Dept. Haematology, Royal Victoria Hosp., Belfast, Northern Ireland
Med Hypotheses; 8(6):627-634 1982

Cellular immune system, fetal and oncofetal antigens, and the maternal-fetal relationship is discussed. Neoplastic transformation is associatied with expression of neoantigens, which are capable of stimulating an immune response, but also with reexpression of fetal antigens which appear to activate a variety of specific and non-specific suppressor mechanisms. In pregnant females and patients with choriocarcinoma, peripheral blood lymphocytes inhibited DNA synthesis of normal lymphocytes thus suggesting that in pregnancy and patients with trophoblastic tumors, altered lymphocyte immunocompetence may play a role in survival of the fetus and neoplasm respectively. (44 Refs)

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